A 21-year-old man is brought to the emergency department by his roommate due to worsening fever, headache, and confusion. The patient recently moved to a dormitory, and his prior medical problems and immunizations are unknown. Temperature is 39.2 C (102.6 F), blood pressure is 98/54 mm Hg, pulse is 112/min, and respirations are 24/min. The patient appears acutely ill. He is obtunded and has nuchal rigidity. Leukocyte count is 19,000/$mm^3$ with 20% band neutrophils. Blood cultures are obtained and lumbar puncture is performed. Gram stain of cerebrospinal fluid reveals gram-negative cocci in pairs. Which of the following is the most likely way that this organism reached the meninges?

A. Middle ear → contiguous tissues → meninges
B. Pharynx → blood → choroid plexus → meninges
C. Pharynx → lymphatic system → meninges
D. Primary lung focus → blood → meninges
E. Traumatic wound → leaking cerebral spinal fluid → meninges

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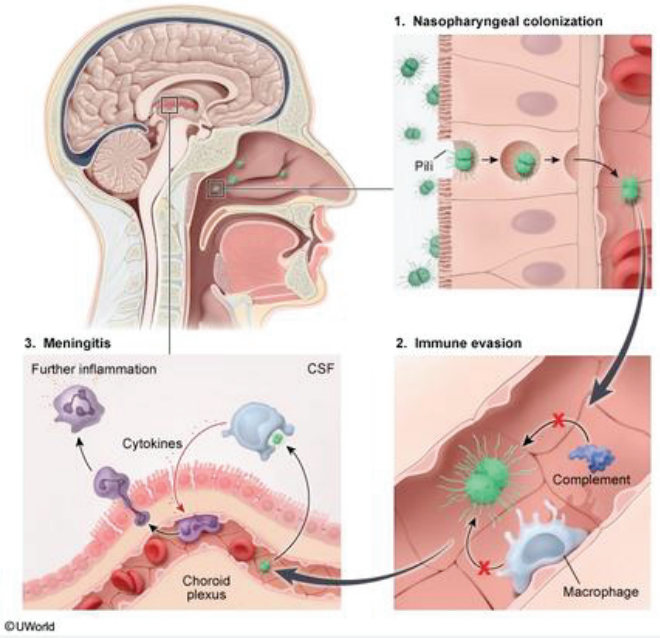
Exhibit Display

Pathogenesis of *Neisseria meningitidis*

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**Acute bacterial meningitis** is a life-threatening infection that classically presents with the triad of fever, nuchal rigidity, and altered mental state. Most cases are caused by *Streptococcus pneumoniae* (gram-positive coccus) and ***Neisseria meningitidis*** (gram-negative diplococcus). These pathogens are transmitted via aerosolized droplets and are able to **colonize the nasopharynx** due to the presence of specialized surface components (eg, fimbriae, pili). Colonization usually leads to an asymptomatic carrier state, but in a minority of patients (~0.2%), the bacteria penetrate the epithelium and enter the **bloodstream**. Intravascular survival is dependent on capsular polysaccharides, which allow the bacteria to evade destruction by the alternative complement system. Meningitis occurs when the bacteria penetrate the cerebral capillary endothelium or the **choroid plexus**, the location of blood-CSF barrier.

**(Choice A)** *Haemophilus influenzae* and *S pneumoniae* can rarely spread into the meninges from a middle ear infection. However, an ear infection is very uncommon cause of meningitis.

**(Choice C)** Spread from the pharynx through the nasal lymphatics to the subarachnoid space may contribute to some cases of bacterial meningitis. However, this route is thought to be far less common than bloodstream invasion with subsequent hematogenous spread.

**(Choice D)** Infections of the lung (eg, *Mycobacterium tuberculosis*, *S pneumoniae*) can lead to bacteremia and meningitis. However, *N meningitidis* does not usually colonize or infect the lung



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**(Choice C)** Spread from the pharynx through the nasal lymphatics to the subarachnoid space may contribute to some cases of bacterial meningitis. However, this route is thought to be far less common than bloodstream invasion with subsequent hematogenous spread.

**(Choice D)** Infections of the lung (eg, *Mycobacterium tuberculosis*, *S pneumoniae*) can lead to bacteremia and meningitis. However, *N meningitidis* does not usually colonize or infect the lung.

**(Choice E)** Traumatic brain injury can lead to CSF leaks, with subsequent infection of the central nervous system. This is particularly common in the setting of basilar skull fracture. *S pneumoniae* (gram-positive cocci in pairs) is the most common organism.

**Educational objective:**

*Neisseria meningitidis* is transmitted primarily by aerosolized droplets and subsequently colonizes the nasopharyngeal epithelium. Penetration of the epithelium can lead to bloodstream infection. Spread to the meninges occurs via transcellular penetration of the cerebral capillary endothelium or entry at the choroid plexus.

| Microbiology | Nervous System | Meningitis |
|---|---|---|
| Subject | System | Topic |

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A 16-year-old girl is brought to the emergency department after she became unresponsive. Temperature is 39.7 C (103.5 F), blood pressure is 70/40 mm Hg, and pulse is 130/min and thready. There is a diffuse petechial and ecchymotic skin rash. Laboratory testing reveals leukocytosis with left shift and evidence of disseminated intravascular coagulation and multiorgan failure. Despite aggressive interventions, the patient dies several hours after admission. Autopsy reveals hemorrhagic necrosis of many internal organs, including the bilateral adrenal glands. Which of the following microbial components is directly responsible for the severity of disease in this patient?

A. Capsular polysaccharide
B. Immunoglobulin protease
C. Lipo-oligosaccharide
D. Lipoteichoic acid
E. Superantigen exotoxin

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A 16-year-old girl is brought to the emergency department after she became unresponsive. Temperature is 39.7 C (103.5 F), blood pressure is 70/40 mm Hg, and pulse is 130/min and thready. There is a diffuse petechial and ecchymotic skin rash. Laboratory testing reveals leukocytosis with left shift and evidence of disseminated intravascular coagulation and multiorgan failure. Despite aggressive interventions, the patient dies several hours after admission. Autopsy reveals hemorrhagic necrosis of many internal organs, including the bilateral adrenal glands. Which of the following microbial components is directly responsible for the severity of disease in this patient?

- A. Capsular polysaccharide (26%)
- B. Immunoglobulin protease (2%)
- C. Lipo-oligosaccharide (47%)
- D. Lipoteichoic acid (4%)
- E. Superantigen exotoxin (18%)

Incorrect



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***Neisseria meningitidis*** is a common cause of rapid-onset sepsis and circulatory collapse in otherwise healthy young individuals. Infections usually start suddenly with myalgias, high fever, headache, and altered level of consciousness and quickly progress to hypotension, organ failure, and death. Many patients also develop a **petechial/ecchymotic rash** due to underlying disseminated intravascular coagulation.

*N meningitidis* has an outer cell membrane virulence factor called **lipo-oligosaccharide** (LOS), which is primarily responsible for the severity of meningococcal disease. LOS, and its close analogue lipopolysaccharide (found in gram-negative enteric rods), are **endotoxins** that cause toxicity when released into the plasma via shedding of the outer membrane ("blebbing") or bacterial lysis. Endotoxins bind to Toll-like receptor 4 on monocytic and dendritic cells and trigger the release of inflammatory cytokines (eg, IL-1, IL-6, TNF-alpha), which leads to endothelial damage, capillary leakage, and hemorrhagic necrosis.

**(Choices A and B)** The capsular polysaccharide of *N meningitidis* is an important virulence factor that helps the bacteria resist phagocytosis and complement activation. *N meningitidis* also releases IgA protease, which aids in nasopharyngeal epithelial colonization. However, these virulence factors are not the direct cause of meningococcal septic shock.


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the direct cause of meningococcal septic shock.

**(Choice D)** Lipoteichoic acid is a major component of the cell wall of most gram-positive bacteria and acts as a regulator of autolytic cell wall enzymes. Although lipoteichoic acid can stimulate the complement cascade, it is not a major cause of septic shock and hemorrhagic inflammation in patients with meningococcemia (a gram-negative organism).

**(Choice E)** Toxic shock syndrome is due to *Staphylococcus aureus* exotoxins, which act as superantigens and result in the wide-spread activation of T-cells (with massive inflammatory cytokine release). Patients usually present with circulatory collapse, organ failure, and erythroderma (a diffuse macular rash that looks like a sunburn). Petechiae and ecchymosis would be atypical.

**Educational objective:**

*Neisseria meningitidis* can cause sepsis and circulatory collapse in previously healthy young individuals. Lipooligosaccharide, a virulence factor in the pathogens outer membrane, is the major underlying cause of disease severity.

**References**

- Neisseria meningitidis: biology, microbiology, and epidemiology.



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A researcher is investigating a new antiseizure drug that binds to and activates GABA-A receptors in the central nervous system. During the experiment, she isolates a nerve and uses a microelectrode to measure its membrane potential under physiologic conditions. The resting potential of the nerve is found to be −70 mV. Which of the following membrane potentials will most likely be recorded from this neuron following exposure to the new drug?

A. −75 mV
B. −70 mV
C. −55 mV
D. 0 mV
E. +25 mV
F. +40 mV
G. +60 mV
H. +125 mV



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measure its membrane potential under physiologic conditions. The resting potential of the nerve is found to be −70 mV. Which of the following membrane potentials will most likely be recorded from this neuron following exposure to the new drug?

- A. −75 mV (74%) ✓
- B. −70 mV (8%)
- C. −55 mV (6%)
- D. 0 mV (2%)
- E. +25 mV (1%)
- F. +40 mV (1%)
- G. +60 mV (3%)
- H. +125 mV (1%)

Correct

74%
57 secs
10/27/2020



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**Equilibration movements of charged ions under physiologic conditions**

| Ion | Charge | Major location | Equilibrium potential | Equilibration movement at -70 mV |
|---|---|---|---|---|
| Sodium | Positive | Extracellular | + 60 mV | Extracellular gradient drives $Na^+$ into cell, making membrane potential more positive |
| Potassium | Positive | Intracellular | - 90 mV | Intracellular gradient drives $K^+$ out of cell, making membrane potential more negative |
| Chloride | Negative | Extracellular | - 75 mV | Extracellular gradient drives $Cl^-$ into cell, making membrane potential more negative |
| Calcium | Positive | Extracellular | + 125 mV | Extracellular gradient drives $Ca^{2+}$ into cell, making membrane potential more positive |



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The **GABA-A receptor** is an ionotropic receptor (eg, part of an ion channel) that regulates the flow of negatively charged **chloride ions** across the neuronal cell membrane. A drug that binds to and activates GABA-A receptors will increase the conductance of chloride ions, causing passive transport down the concentration gradient into the cell interior. This causes the membrane potential to become **hyperpolarized** (more negative than the resting membrane potential) by approaching or reaching the **equilibrium potential** for chloride (−75 mV). A cell that becomes hyperpolarized is temporarily made refractory to firing an action potential.

**(Choice B)** Exposure to the experimental drug will make the neuronal membrane potential more negative than the resting membrane potential due to the opening of chloride channels.

**(Choice C)** The opening of ligand-gated (controlled by binding of neurotransmitters) sodium channels allows for the initial influx of positively charged sodium ions. This causes a graded depolarization of the neuronal cell membrane toward the threshold for firing an action potential (−55 mV).

**(Choices D, E, F, and G)** Once the threshold membrane potential is reached, fast voltage-gated sodium channels open to mediate the upstroke phase of the neuronal action potential. During this time, the membrane potential becomes even more positive due to the rapid influx of sodium ions and causes the membrane potential to approach the equilibrium potential for sodium (+60 mV).


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**(Choices D, E, F, and G)** Once the threshold membrane potential is reached, fast voltage-gated sodium channels open to mediate the upstroke phase of the neuronal action potential. During this time, the membrane potential becomes even more positive due to the rapid influx of sodium ions and causes the membrane potential to approach the equilibrium potential for sodium (+60 mV).

**(Choice H)** The influx of positively charged calcium ions can raise the membrane potential even further (more positive than +60 mV) toward the equilibrium potential for calcium ions (+125 mV).

**Educational objective:**

A drug that binds to and activates GABA-A receptors (or enhances their activity) will increase the conductance of chloride ions, leading to increased passive transport of chloride into the cell interior. This causes the membrane potential to become hyperpolarized (more negative than the resting membrane potential) by approaching or reaching the equilibrium potential for chloride.

**References**

- Generation of resting membrane potential.

| Physiology | Nervous System | Resting membrane potential and action potential |
|---|---|---|
| Subject | System | Topic |



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A 45-year-old man comes to the office for follow-up. He was diagnosed with focal epilepsy 2 years ago and has been treated with several antiepileptic medications. Over the last 6 months, his seizure frequency has increased despite compliance with medical therapy. Neurologic examination and brain imaging are unremarkable. The patient is started on a new antiepileptic medication that selectively blocks voltage-gated calcium channels. This medication most likely affects which of the following steps of neurotransmission?

A. Axonal propagation of the action potential
B. Axonal transport of the neurotransmitter vesicles
C. Fusion and release of neurotransmitter vesicles
D. Neurotransmitter synthesis and packaging into vesicles
E. Release of calcium from the endoplasmic reticulum

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A 45-year-old man comes to the office for follow-up. He was diagnosed with focal epilepsy 2 years ago and has been treated with several antiepileptic medications. Over the last 6 months, his seizure frequency has increased despite compliance with medical therapy. Neurologic examination and brain imaging are unremarkable. The patient is started on a new antiepileptic medication that selectively blocks voltage-gated calcium channels. This medication most likely affects which of the following steps of neurotransmission?

A. Axonal propagation of the action potential (7%)
B. Axonal transport of the neurotransmitter vesicles (4%)
✓ C. Fusion and release of neurotransmitter vesicles (76%)
D. Neurotransmitter synthesis and packaging into vesicles (3%)
E. Release of calcium from the endoplasmic reticulum (8%)

Correct

76% Answered correctly

01 min, 05 secs Time Spent

09/27/2020 Last Updated



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Neurons communicate with each other via synapses, regions where the axon terminal of a presynaptic neuron transmits chemical signals to the dendrites of a postsynaptic neuron. Binding of an excitatory neurotransmitter (eg, glutamate) to a postsynaptic neuron causes opening of ligand-gated sodium channels, leading to sodium influx and membrane depolarization. This depolarization impulse is transmitted from the dendrites through the cell body to the axon hillock, which contains a large number of voltage-gated sodium channels. Once the axon hillock becomes sufficiently depolarized, an action potential is triggered and propagates along the axon via a steady influx of sodium ions. When the action potential reaches the axon terminal, **voltage-gated calcium channels** open and allow the influx of calcium, which is essential for the fusion and **release** of neurotransmitter vesicles into the synaptic cleft.

Seizures occur due to abnormal, synchronized firing of hyperexcitable neurons in the brain, and many antiepileptic medications work by modifying electrochemical transmission between neurons. Gabapentin is an anticonvulsant that works by inhibiting presynaptic voltage-gated calcium channels, whereas levetiracetam acts downstream by disrupting vesicle fusion.

**(Choice A)** Antiepileptic medications such as phenytoin and carbamazepine disrupt the generation and propagation of action potentials (in the axon hillock and axon proper, respectively) by blocking voltage-gated sodium channels.


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propagation of action potentials (in the axon hillock and axon proper, respectively) by blocking voltage-gated sodium channels.

**(Choices B and D)** Neurotransmitters are synthesized in the presynaptic neuronal cell body and transported to the axon terminal (via kinesin motor proteins), where they are packaged in synaptic vesicles and primed for release.

**(Choice E)** Although the endoplasmic reticulum contains calcium release channels, these do not directly participate in neurotransmission. Release of calcium from the endoplasmic reticulum is more important for skeletal muscle contraction.

**Educational objective:**
Voltage-gated sodium channels are important for the generation and propagation of action potentials. When the action potential reaches the axon terminal, voltage-gated calcium channels open and allow the influx of calcium, which is essential for the fusion and release of neurotransmitter vesicles into the synaptic cleft.

**References**

- Targets for antiepileptic drugs in the synapse.
- Research advances in basic mechanisms of seizures and antiepileptic drug action



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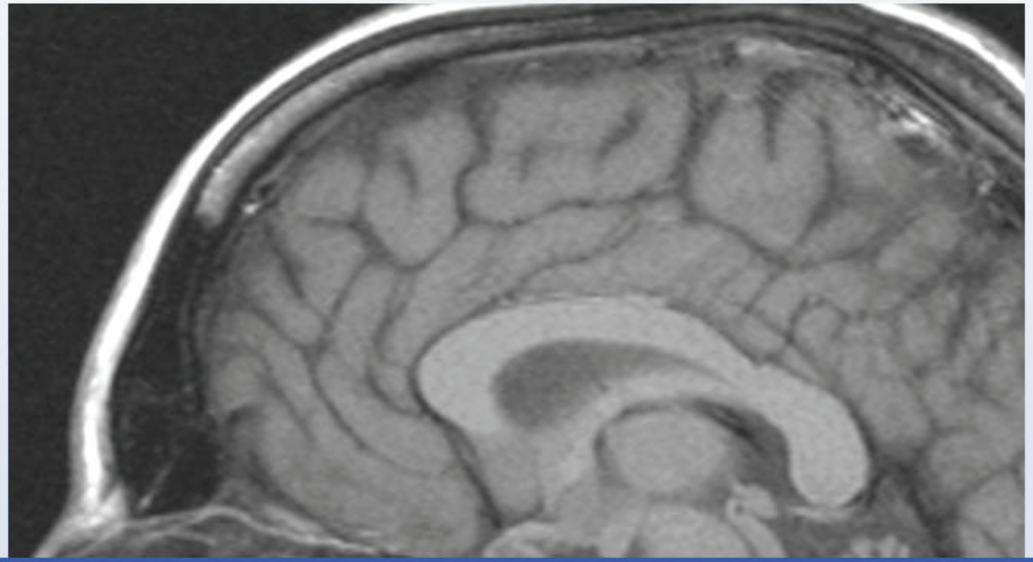
A 38-year-old woman is brought to the emergency department after a motor vehicle collision. She sustained no injuries in the collision but is adamant that she did not see the car that hit her along the front side of her vehicle. The patient also reports that she has been having daily headaches and has not menstruated in 4 months. On physical examination, there is bitemporal hemianopsia but no other abnormalities. MRI of the brain is shown below.





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menstruated in 4 months. On physical examination, there is bitemporal hemianopsia but no other

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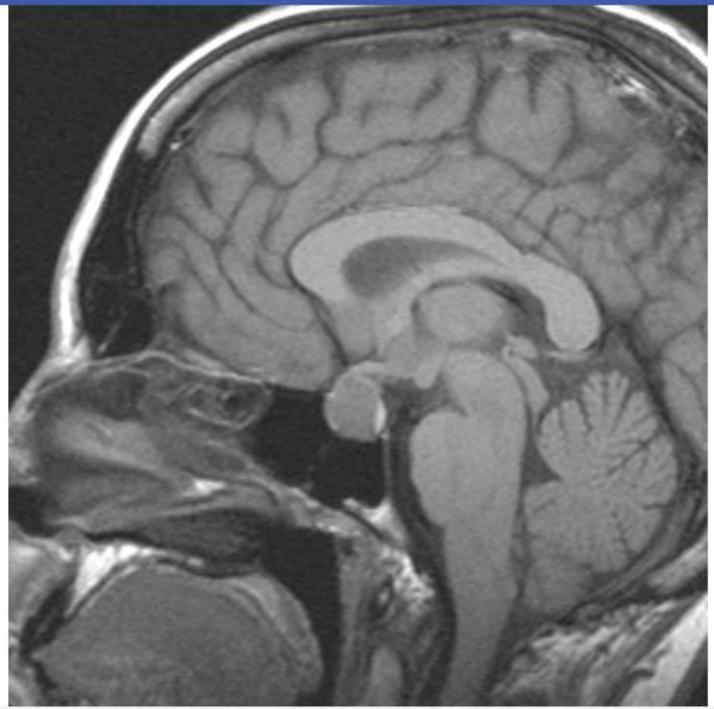

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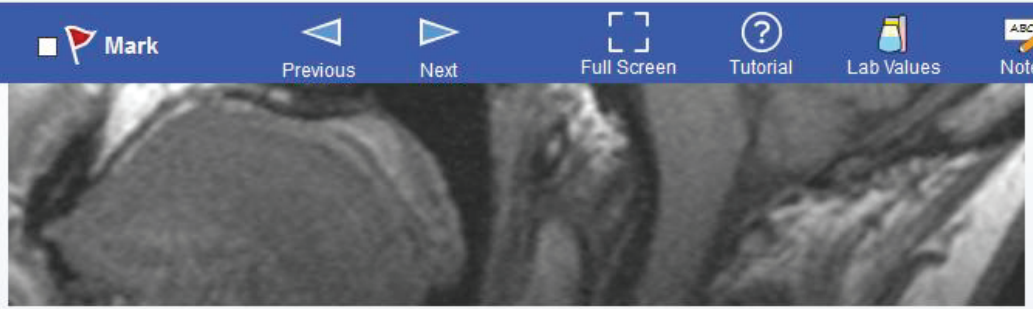

This patient's lesion most likely originates from which of the following embryologic layers?

A. Endoderm
B. Mesoderm
C. Neural crest
D. Neural tube
E. Notochord
F. Surface ectoderm

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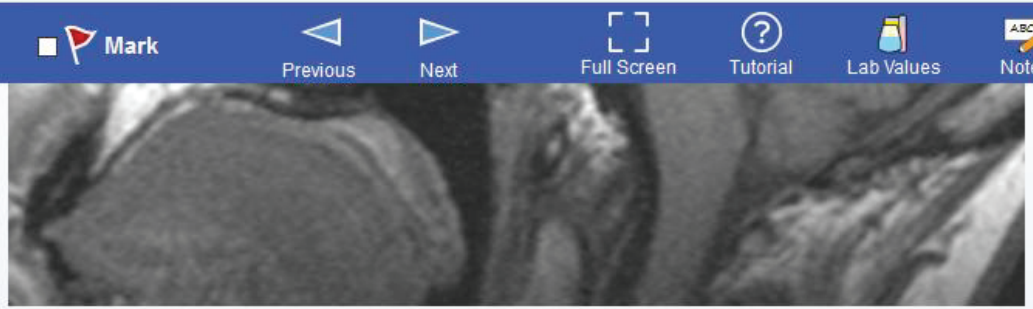

This patient's lesion most likely originates from which of the following embryologic layers?

- A. Endoderm (9%)
- B. Mesoderm (6%)
- C. Neural crest (21%)
- D. Neural tube (13%) ✗
- E. Notochord (1%)
- F. Surface ectoderm (47%) ✓

Incorrect
Correct answer

47%

01 min, 23 secs

12/28/2020



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| Embryological derivatives | | |
|---|---|---|
| Ectoderm | Surface ectoderm | • Anterior pituitary (Rathke pouch)<br>• Lens & cornea<br>• Inner ear sensory organs, olfactory epithelium<br>• Nasal & oral epithelial linings, salivary glands<br>• Epidermis, sweat & mammary glands |
| | Neural tube | • Brain & spinal cord<br>• Posterior pituitary, pineal gland<br>• Retina |
| | Neural crest | • Neural ganglia, adrenal medulla<br>• Schwann cells; pia & arachnoid mater<br>• Aorticopulmonary septum & endocardial cushions<br>• Branchial arches (bones & cartilage)<br>• Skull bones |


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| | | |
|---|---|---|
| | Neural crest | • Neural ganglia, adrenal medulla<br>• Schwann cells; pia & arachnoid mater<br>• Aorticopulmonary septum & endocardial cushions<br>• Branchial arches (bones & cartilage)<br>• Skull bones<br>• Melanocytes |
| Mesoderm | | • Muscles (skeletal, cardiac & smooth)<br>• Connective tissue, bone & cartilage<br>• Serosal linings (eg, peritoneum)<br>• Cardiovascular & lymphatic system<br>• Spleen & hemopoietic cells<br>• Kidney & ureters, internal genitalia<br>• Adrenal cortex |
| Endoderm | | • Gastrointestinal tract, liver, pancreas<br>• Lungs<br>• Thymus, parathyroids, thyroid follicular cells<br>• Middle ear epithelium |



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| | |
|---|---|
| Mesoderm | • Muscles (skeletal, cardiac & smooth)<br>• Connective tissue, bone & cartilage<br>• Serosal linings (eg, peritoneum)<br>• Cardiovascular & lymphatic system<br>• Spleen & hemopoietic cells<br>• Kidney & ureters, internal genitalia<br>• Adrenal cortex |
| Endoderm | • Gastrointestinal tract, liver, pancreas<br>• Lungs<br>• Thymus, parathyroids, thyroid follicular cells<br>• Middle ear epithelium<br>• Bladder & urethra<br>• Parafollicular (C) cells* |

*Formerly thought to be of neural crest origin.

Bitemporal hemianopsia, amenorrhea, and enlargement of the pituitary gland on brain imaging are suggestive of a prolactin-secreting **pituitary adenoma**. Prolactinomas develop from lactotroph cells in the



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Bitemporal hemianopsia, amenorrhea, and enlargement of the pituitary gland on brain imaging are suggestive of a prolactin-secreting **pituitary adenoma**. Prolactinomas develop from lactotroph cells in the **anterior pituitary** (adenohypophysis).

All tissues can be traced back to 3 primary germ layers: ectoderm, mesoderm, and endoderm. These germ layers form during the process of gastrulation, which occurs during week 3 of embryogenesis. Gastrulation is initiated by formation of the primitive streak, a thickening of the epiblast cell layer that appears at the caudal end of the embryo and grows cranially. Epiblast cells then undergo an epithelial-to-mesenchymal transition, causing them to lose their cell-cell adhesion properties. This allows them to migrate downward through the primitive streak to form the mesoderm **(Choice B)** and endoderm **(Choice A)** layers. The remainder of the epiblast layer forms the ectoderm.

About 2 days after gastrulation begins, some of the epiblast cells migrate cranially through the primitive node (the cephalic end of the primitive streak) to form a midline cellular cord known as the notochord. The notochord induces the overlying ectoderm to differentiate into the neuroectoderm and form the neural plate. The neural plate gives rise to the neural crest and neural tube cells **(Choices C and D)**, while the remainder of the ectoderm becomes the surface ectoderm. The anterior pituitary is derived from the **Rathke pouch**, an evagination of the surface ectoderm that lines the fetal oral cavity. In contrast, the



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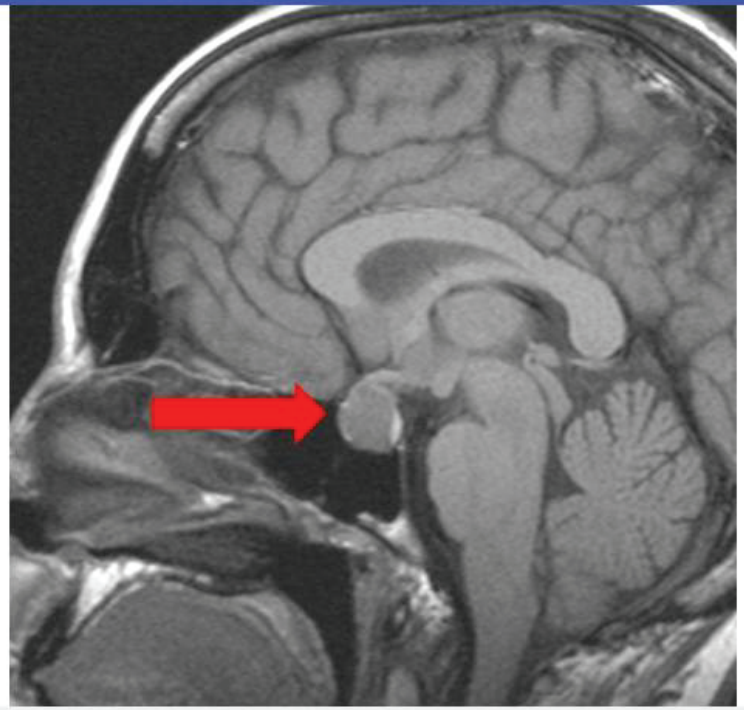

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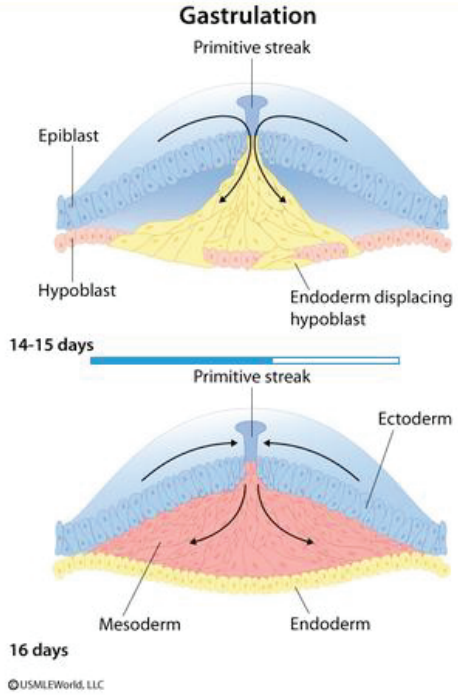


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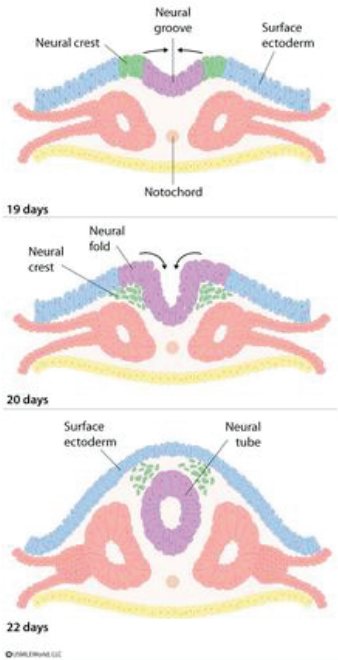
## Exhibit Display

### Neural tube formation

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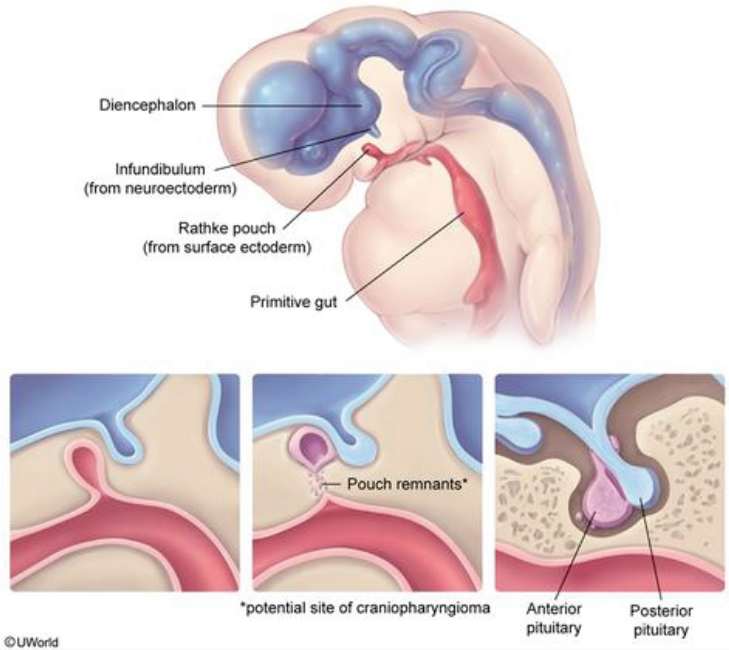
## Exhibit Display

### Pituitary embryology

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About 2 days after gastrulation begins, some of the epiblast cells migrate cranially through the primitive node (the cephalic end of the primitive streak) to form a midline cellular cord known as the notochord. The notochord induces the overlying ectoderm to differentiate into the neuroectoderm and form the neural plate. The neural plate gives rise to the neural crest and neural tube cells **(Choices C and D)**, while the remainder of the ectoderm becomes the surface ectoderm. The anterior pituitary is derived from the **Rathke pouch**, an evagination of the surface ectoderm that lines the fetal oral cavity. In contrast, the posterior pituitary (pars nervosa and pituitary stalk) is derived from the infundibulum, an extension of neuroectoderm from the diencephalon.

**(Choice E)** The notochord becomes the nucleus pulposus of the intervertebral disks in adults.

**Educational objective:**

All adult cells and tissues can be traced back to the 3 primary germ layers: ectoderm, mesoderm, and endoderm. The ectoderm gives rise to the surface ectoderm, neural tube, and neural crest.

| Embryology | Nervous System | Pituitary adenoma |
|---|---|---|
| Subject | System | Topic |

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A 4-day-old girl is brought to the office for a routine newborn visit. She was born at 39 weeks gestation via normal spontaneous vaginal delivery to a gravida 5 para 4 woman. The patient has been breastfed exclusively but has had increasing difficulty feeding over the past 24 hours. Her parents say that she is "too sleepy to feed" and has been vomiting. The infant has 3 healthy, living siblings and a brother who died in infancy from "low sugar in his blood." Physical examination shows tachypnea and signs of dehydration. The patient is responsive to painful stimuli only. After acute treatment and stabilization, urine testing reveals significantly elevated levels of methylmalonic acid. Which of the following sets of laboratory values would most likely result from this patient's condition?

| | Urine propionic acid | Serum glucose | Urine ketones | Serum ammonia |
|---|---|---|---|---|
| A. | Normal | ↓ | ↑ | Normal |
| B. | ↑ | ↓ | ↑ | ↑ |
| C. | Normal | ↓ | Negative | ↑ |



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| | Urine propionic acid | Serum glucose | Urine ketones | Serum ammonia |
|---|---|---|---|---|
| A. | Normal | ↓ | ↑ | Normal |
| B. | ↑ | ↓ | ↑ | ↑ |
| C. | Normal | ↓ | Negative | ↑ |
| D. | Normal | Normal | Negative | ↑ |
| E. | Normal | ↓ | ↑ | ↓ |

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too sleepy to feed" and has been vomiting. The infant has 3 healthy, living siblings and a brother who died in infancy from "low sugar in his blood." Physical examination shows tachypnea and signs of dehydration. The patient is responsive to painful stimuli only. After acute treatment and stabilization, urine testing reveals significantly elevated levels of methylmalonic acid. Which of the following sets of laboratory values would most likely result from this patient's condition?

| | Urine propionic acid | Serum glucose | Urine ketones | Serum ammonia | |
|---|---|---|---|---|---|
| A. | Normal | ↓ | ↑ | Normal | (15%) |
| ✓ B. | ↑ | ↓ | ↑ | ↑ | (47%) |
| C. | Normal | ↓ | Negative | ↑ | (26%) |
| D. | Normal | Normal | Negative | ↑ | (3%) |
| E. | Normal | ↓ | ↑ | ↓ | (7%) |


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Explanation

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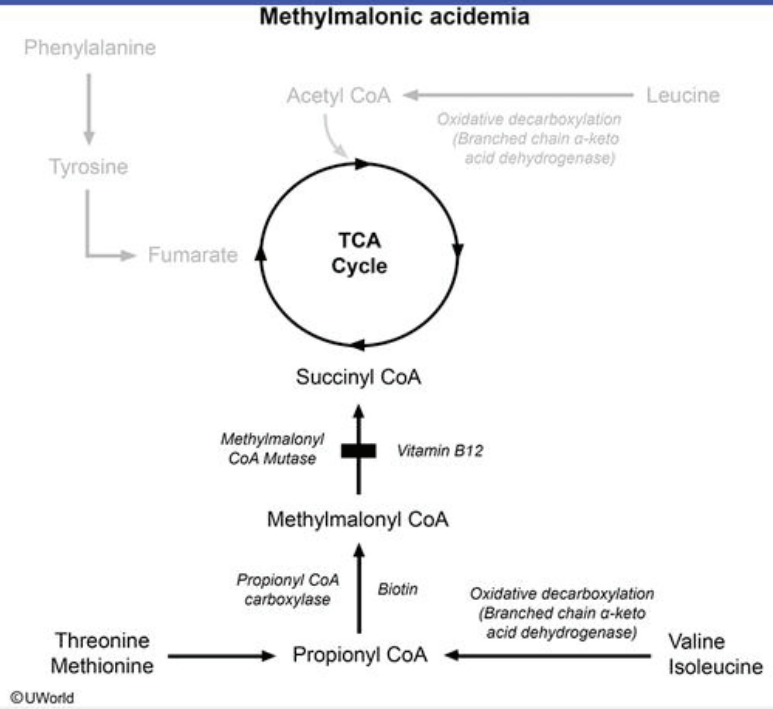


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Methionine Isoleucine

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This patient's presentation is consistent with methylmalonic acidemia, an **autosomal recessive organic acidemia** resulting from complete or partial deficiency of the enzyme **methylmalonyl-CoA mutase**.

Catabolism of isoleucine, valine, threonine, methionine, and odd-chain fatty acids normally leads to formation of propionyl CoA, which is then converted to methylmalonyl CoA by biotin-dependent carboxylation. Isomerization of methylmalonyl CoA through a vitamin B12-dependent reaction forms succinyl CoA, which subsequently enters the TCA cycle. Mutations in methylmalonyl-CoA mutase result in buildup of methylmalonic acid and propionic acid, leading to a **metabolic acidosis**. **Hypoglycemia** results from overall increased metabolic rate leading to increased glucose utilization and direct toxic inhibition of gluconeogenesis by the organic acids. The presence of hypoglycemia leads to increased free fatty acid metabolism that produces **ketones**, resulting in a further anion gap metabolic acidosis. Finally, organic acids also directly inhibit the urea cycle, leading to **hyperammonemia**.

Complete deficiency of methylmalonyl-CoA mutase results in an anion gap metabolic acidosis, hypoglycemia, ketosis, and hyperammonemia. These metabolic derangements manifest as hypotonia, lethargy, vomiting, and respiratory distress (tachypnea due to acidosis) in the neonatal period. Diagnosis is confirmed by the presence of **elevated urine methylmalonic acid and propionic acid**.



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confirmed by the presence of **elevated urine methylmalonic acid and propionic acid**.

Propionic acidemia, a deficiency in propionyl-CoA carboxylase, also results in hyperammonemia, hypoglycemia, and metabolic acidosis, although it does not display elevated levels of urine methylmalonic acid.

**(Choice A)** Production of ketones in the presence of hypoglycemia is an appropriate response in the fasting state, as ketones provide fuel for the brain. In this patient, the notable family history and elevated serum methylmalonic acid level make methylmalonic acidemia more likely than simple fasting or dehydration.

**(Choice C)** Fatty acid oxidation disorders, such as medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, can present with hypoglycemia, hyperammonemia, and metabolic acidosis, but these disorders lack an appropriate ketosis.

**(Choice D)** Urea cycle defects typically present with hyperammonemia without hypoglycemia or ketosis.

**(Choice E)** Propionic acid levels are elevated in patients with methylmalonic acidemia due to downstream enzymatic deficiency of methylmalonyl-CoA mutase.

**Educational objective:**

Methylmalonic acidemia is an organic acidemia due to complete or partial deficiency of methylmalonyl-CoA


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serum methylmalonic acid level make methylmalonic acidemia more likely than simple fasting or dehydration.

**(Choice C)** Fatty acid oxidation disorders, such as medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, can present with hypoglycemia, hyperammonemia, and metabolic acidosis, but these disorders lack an appropriate ketosis.

**(Choice D)** Urea cycle defects typically present with hyperammonemia without hypoglycemia or ketosis.

**(Choice E)** Propionic acid levels are elevated in patients with methylmalonic acidemia due to downstream enzymatic deficiency of methylmalonyl-CoA mutase.

**Educational objective:**

Methylmalonic acidemia is an organic acidemia due to complete or partial deficiency of methylmalonyl-CoA mutase. Complete deficiency classically presents with lethargy, vomiting, and tachypnea in a newborn. Laboratory testing shows hyperammonemia, ketotic hypoglycemia, and metabolic acidosis. The diagnosis is confirmed by elevated urine methylmalonic acid and propionic acid.

**References**

- Proposed guidelines for the diagnosis and management of methylmalonic and propionic acidemia.



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A 16-year-old boy with mild intellectual disability is brought to the office to be evaluated for attention deficit-hyperactivity disorder. The parents state that he has always been impulsive and inattentive and that teachers are concerned about his inattentiveness and poor grades. Review of medical records shows a history of gross motor and speech delay for which he received physical and speech therapies during childhood. On physical examination, the boy has a long and narrow face, a prominent mandible, and large testes. There is hyperlaxity of his finger and thumb joints. Which of the following is the most likely diagnosis in this patient?

A. Down syndrome mosaicism
B. Ehlers-Danlos syndrome
C. Fragile X syndrome
D. Klinefelter syndrome
E. Marfan syndrome
F. Prader-Willi syndrome


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hyperactivity disorder. The parents state that he has always been impulsive and inattentive and that teachers are concerned about his inattentiveness and poor grades. Review of medical records shows a history of gross motor and speech delay for which he received physical and speech therapies during childhood. On physical examination, the boy has a long and narrow face, a prominent mandible, and large testes. There is hyperlaxity of his finger and thumb joints. Which of the following is the most likely diagnosis in this patient?

A. ~~Down syndrome mosaicism~~ (0%)
B. ~~Ehlers-Danlos syndrome~~ (9%)
C. Fragile X syndrome (79%)
D. Klinefelter syndrome (3%)
E. Marfan syndrome (5%)
F. Prader-Willi syndrome (2%)

Correct
79%
55 secs
01/08/2021


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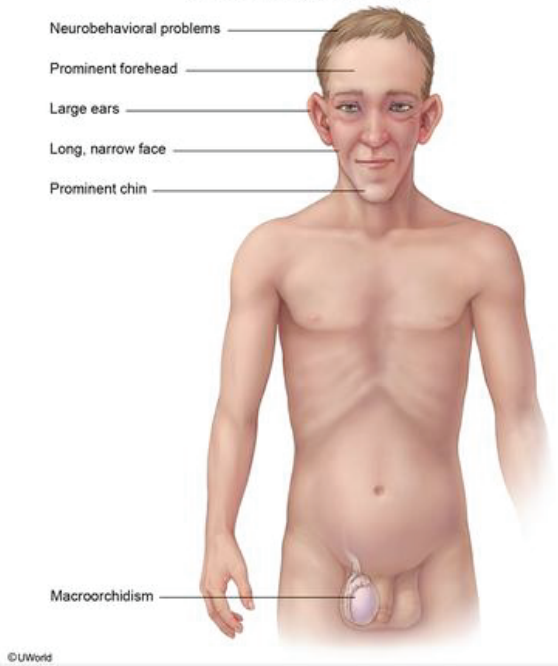
## Exhibit Display

**Features of fragile X syndrome**

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This patient has **fragile X syndrome** (FXS), the most common inherited and the second most common congenital cause of **intellectual disability**. FXS is an **X-linked** disorder caused by a loss-of-function mutation in the fragile X mental retardation 1 (*FMR1*) gene on the long arm of the X chromosome. Males who inherit the full mutation will manifest the features of FXS, whereas females with one abnormal X chromosome will have a milder and variable presentation.

The clinical features of FXS are most apparent after puberty in males; affected individuals have a **long, narrow face**, a **prominent forehead** and **chin**, and **large testes**. Patients often have **hyperlaxity** of the joints in the hand. **Developmental delay** (speech and motor) is common in infancy, but **neuropsychiatric features** often present in childhood (eg, anxiety, attention deficit-hyperactivity disorder, autism spectrum disorder).

**(Choice A)** Down syndrome, or trisomy 21, is the most common cause of congenital intellectual disability. In patients with Down syndrome mosaicism, some cells (but not all) have an extra copy of chromosome 21. These patients may have a milder presentation than those with classic Down syndrome.

**(Choice B)** Ehlers-Danlos syndrome is a connective tissue disorder that is most commonly due to defective type V collagen production. Patients typically have skin hyperelasticity and fragility as well as



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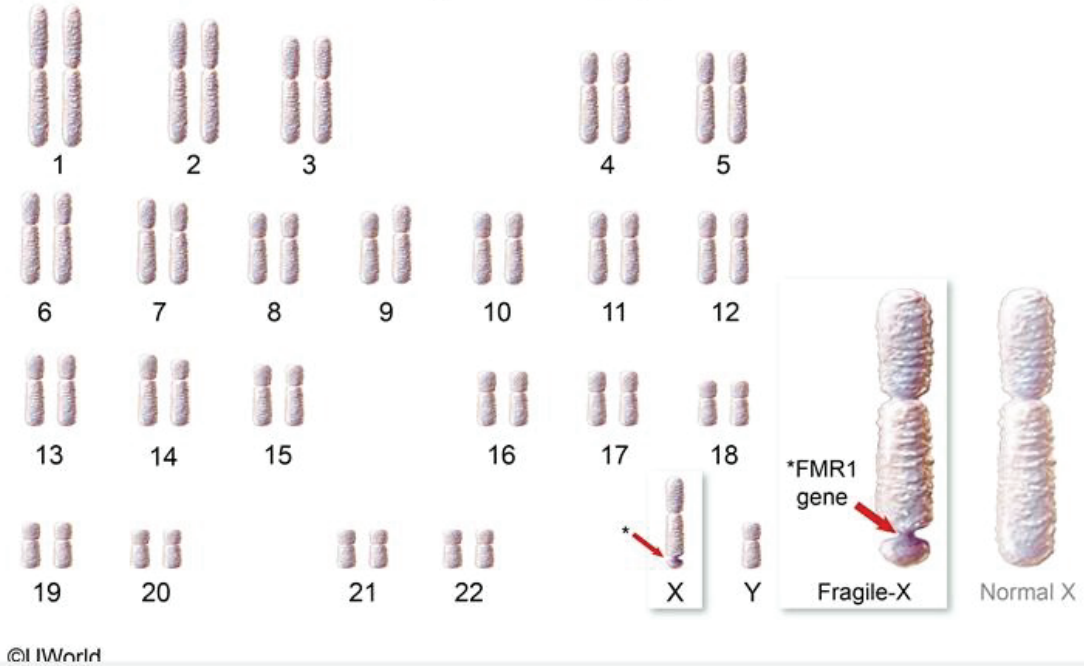
Exhibit Display

## Fragile X karyotype

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defective type V collagen production. Patients typically have skin hyperelasticity and fragility as well as



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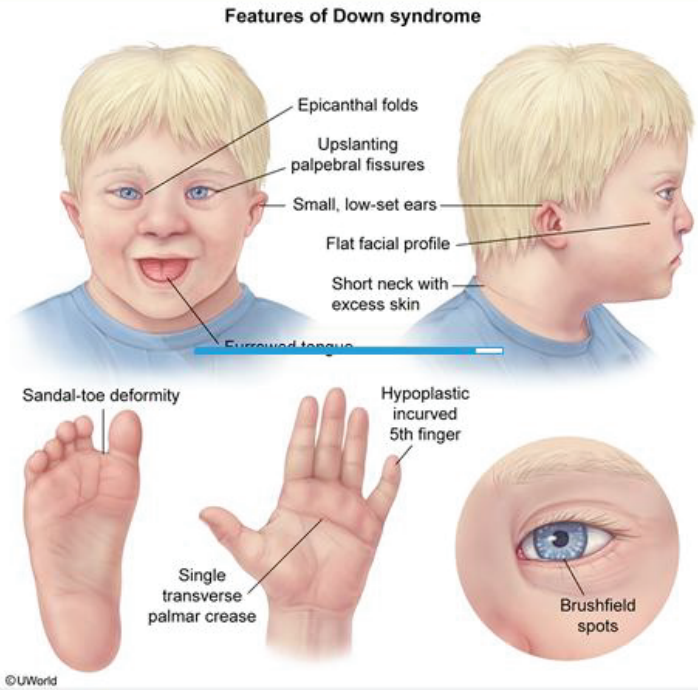


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defective type V collagen production. Patients typically have skin hyperelasticity and fragility as well as



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21. These patients may have a milder presentation than those with classic Down syndrome.

**(Choice B)** Ehlers-Danlos syndrome is a connective tissue disorder that is most commonly due to defective type V collagen production. Patients typically have skin hyperelasticity and fragility as well as joint hyperlaxity. Ehlers-Danlos syndrome is not associated with intellectual disability.

**(Choice D)** Patients with Klinefelter syndrome (47,XXY) often have mild intellectual disability in addition to tall stature, gynecomastia, small testes (often undescended), and infertility.

**(Choice E)** Marfan syndrome is an autosomal dominant connective tissue disorder characterized by tall stature, arachnodactyly (long and thin fingers), ectopia lentis (lens displacement), and dilation of the proximal aorta. Intellectual disability is not associated with Marfan syndrome.

**(Choice F)** Prader-Willi syndrome is an imprinting disorder caused by a paternal deletion of part of chromosome 15. In infancy, hypotonia and hyperphagia lead to gross motor delays and obesity, respectively. Intellectual disability and behavioral problems (eg, autistic-like behaviors, obsessive compulsive features) are common.

**Educational objective:**
Fragile X syndrome is an X-linked disorder that presents with a long, narrow face, a prominent chin and forehead, and large testes. Patients often have developmental delay and neuropsychiatric findings that


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21. These patients may have a milder presentation than those with classic Down syndrome

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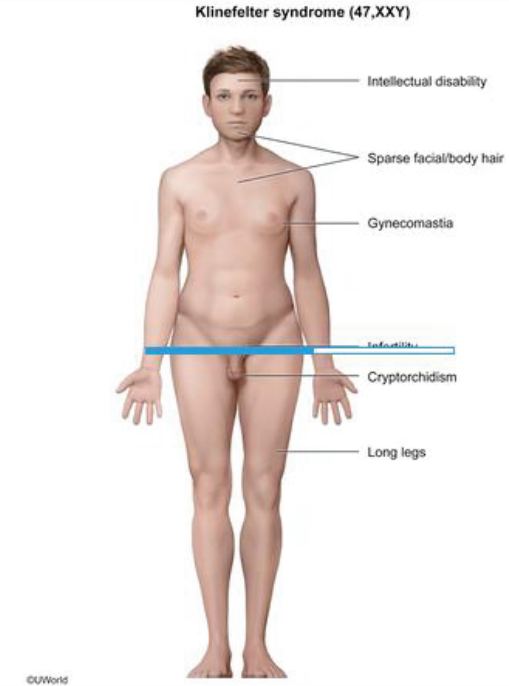


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forehead, and large testes. Patients often have developmental delay and neuropsychiatric findings that



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21. These patients may have a milder presentation than those with classic Down syndrome

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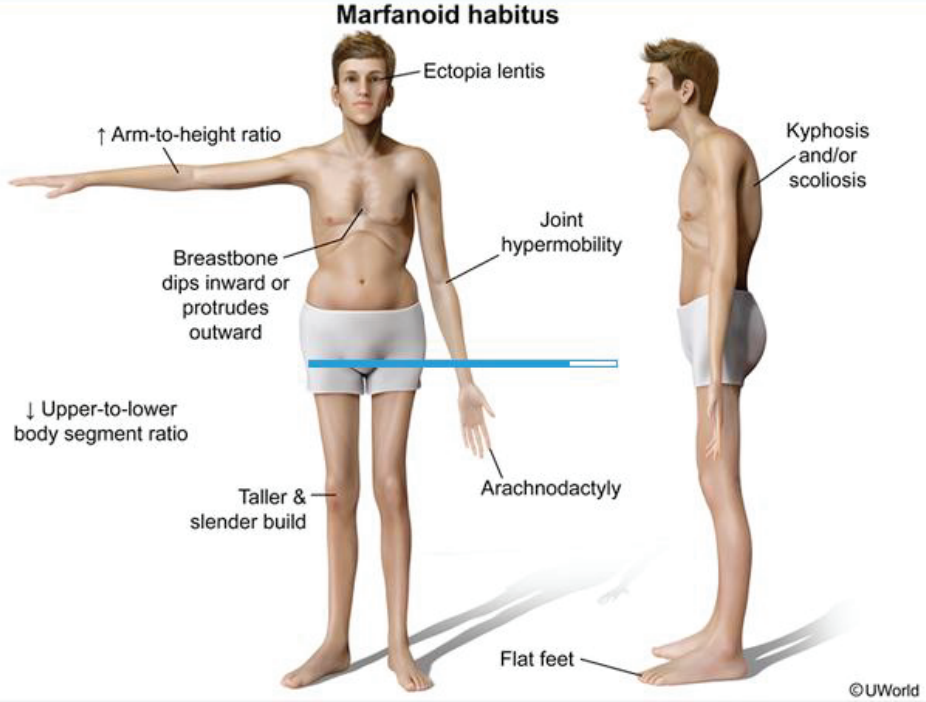


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**(Choice F)** Prader-Willi syndrome is an imprinting disorder caused by a paternal deletion of part of chromosome 15. In infancy, hypotonia and hyperphagia lead to gross motor delays and obesity, respectively. Intellectual disability and behavioral problems (eg, autistic-like behaviors, obsessive compulsive features) are common.

**Educational objective:**

Fragile X syndrome is an X-linked disorder that presents with a long, narrow face, a prominent chin and forehead, and large testes. Patients often have developmental delay and neuropsychiatric findings that overlap with anxiety disorders, autism, and attention deficit-hyperactivity disorder.

**References**

- Fragile X syndrome.

| Genetics | Nervous System | Fragile x syndrome |
|---|---|---|
| Subject | System | Topic |



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A 41-year-old man with trisomy 21 is evaluated in the clinic due to cognitive decline. The patient has a history of moderate intellectual disability, but his higher cognitive functions have become progressively impaired in the past several years. He previously volunteered at a community library but recently lost his position as he could no longer perform his duties. The patient is now completely dependent on a caregiver for assistance with his activities of daily living such as getting dressed, bathing, and using the toilet. The patient keeps wandering in the group home and has become lost on several occasions. Which of the following is most likely to be increased in this patient?

A. Amyloid A protein
B. Amyloid precursor protein
C. Apolipoprotein E epsilon 4
D. CAG trinucleotide repeats
E. Islet amyloid polypeptide

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A 41-year-old man with trisomy 21 is evaluated in the clinic due to cognitive decline. The patient has a history of moderate intellectual disability, but his higher cognitive functions have become progressively impaired in the past several years. He previously volunteered at a community library but recently lost his position as he could no longer perform his duties. The patient is now completely dependent on a caregiver for assistance with his activities of daily living such as getting dressed, bathing, and using the toilet. The patient keeps wandering in the group home and has become lost on several occasions. Which of the following is most likely to be increased in this patient?

- A. Amyloid A protein (11%)
- ✓ B. Amyloid precursor protein (62%)
- C. Apolipoprotein E epsilon 4 (23%)
- D. ~~CAG trinucleotide repeats~~ (1%)
- E. Islet amyloid polypeptide (1%)

62%  01 min, 42 secs  01/17/2021


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| Down syndrome comorbidities | |
|---|---|
| **Neurology** | • Intellectual disability<br>• Early-onset Alzheimer disease |
| **Cardiology** | • Complete atrioventricular septal defect<br>• Ventricular septal defect<br>• Atrial septal defect |
| **Gastroenterology** | • Duodenal atresia<br>• Hirschsprung disease |
| **Endocrinology** | • Hypothyroidism<br>• Type 1 diabetes mellitus<br>• Obesity |
| **Hematology** | • Acute leukemia |
| **Rheumatology** | • Atlantoaxial instability |


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**Trisomy 21**, also known as Down syndrome, is the most commonly diagnosed chromosomal anomaly in liveborn neonates. Typical symptoms include intellectual disability, congenital abnormalities (eg, gastrointestinal, cardiac), physical growth delay, and characteristic facial features (eg, flat facies, protruding tongue, epicanthic folds, oblique palpebral fissures). Many patients with trisomy 21 develop **early-onset Alzheimer disease (AD)**, defined as diagnosis of AD age ≤65, with some developing AD as early as the fourth decade of life.

Characteristic pathologic changes associated with AD involve accumulation of intracellular neurofibrillary tangles and extracellular amyloid-beta plaques:

- Neurofibrillary tangles are composed of tau protein, a primary component of intracellular microtubules. In AD, tau protein is hyperphosphorylated, causing microtubule structures to collapse into "tangles" that contribute to global neuronal dysfunction.
- Amyloid beta is an abnormal fragment of **amyloid precursor protein**, which is normally involved in synaptic formation and repair. In AD, the protein is not properly cleared and forms amyloid fragments; these then harden into insoluble plaques that accumulate in brain tissue and vessel walls.

The amyloid precursor protein (*APP*) gene is located on **chromosome 21**. The **extra copy of *APP*** present in trisomy 21 is thought to accelerate amyloid accumulation and lead to early-onset AD.


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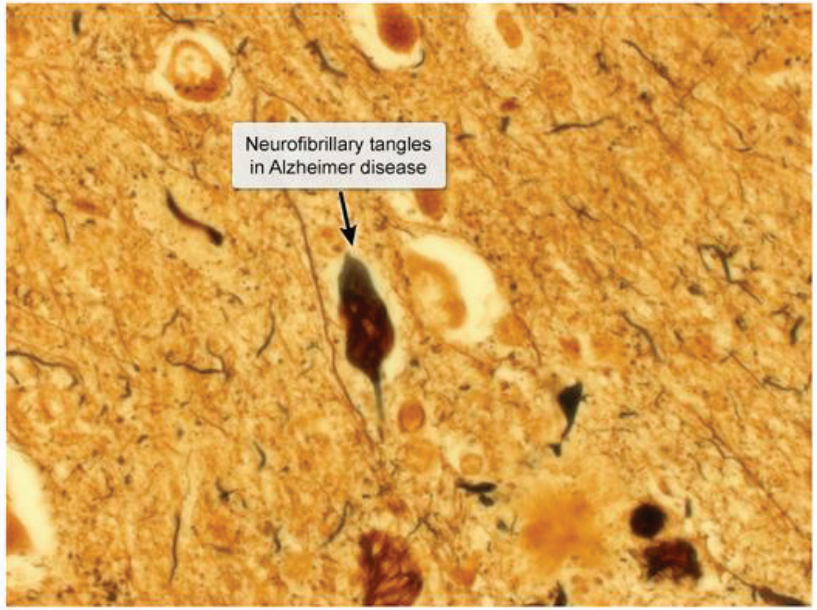
Exhibit Display

Alzheimer disease

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present in trisomy 21 is thought to accelerate amyloid accumulation and lead to early-onset AD.



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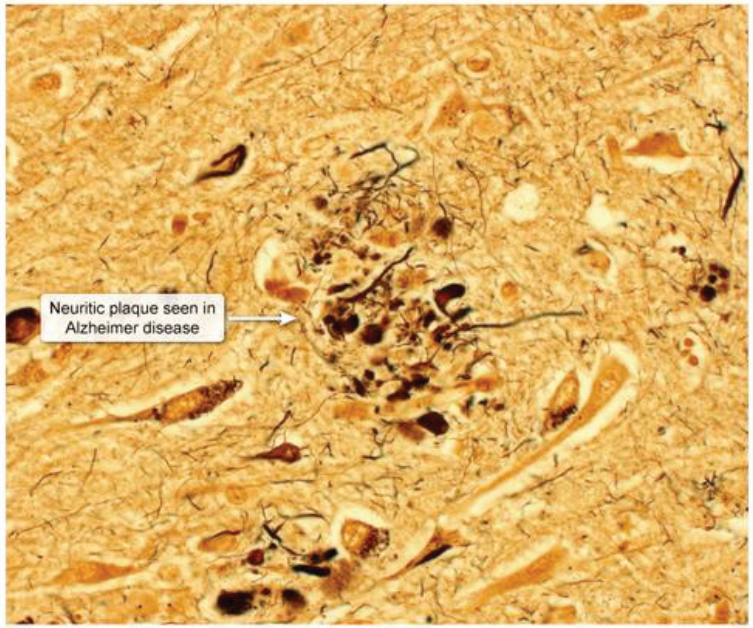
## Exhibit Display

**Alzheimer disease**

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these then harden into insoluble plaques that accumulate in brain tissue and vessel walls.

The amyloid precursor protein (*APP*) gene is located on **chromosome 21**. The **extra copy of *APP*** present in trisomy 21 is thought to accelerate amyloid accumulation and lead to early-onset AD.

**(Choice A)** Amyloid A protein is an acute-phase reactant that is associated with the development of multisystemic amyloidosis (AA amyloidosis) in reaction to chronic disease states (eg, rheumatoid arthritis, inflammatory bowel disease).

**(Choice C)** Apolipoprotein E is found in 3 allelic variations: epsilon 2, 3, and 4. Those with 1 or 2 copies of the epsilon 4 allele are at greater risk for late-onset AD (ie, AD diagnosed at age >65) compared with those without the allele.

**(Choice D)** Expansion of CAG trinucleotide repeats in the *HTT* gene, which codes for huntingtin protein, is responsible for Huntington disease. Individuals with this condition typically have movement abnormalities (eg, chorea), psychiatric symptoms, and dementia.

**(Choice E)** Islet amyloid polypeptide is a normal secretory product of pancreatic beta cells that forms cytotoxic deposits in type 2 diabetes mellitus, impairing beta-cell function.

**Educational objective:**

Patients with trisomy 21 (Down syndrome) have 3 copies of the amyloid precursor protein gene located on


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**(Choice C)** Apolipoprotein E is found in 3 allelic variations: epsilon 2, 3, and 4. Those with 1 or 2 copies of the epsilon 4 allele are at greater risk for late-onset AD (ie, AD diagnosed at age >65) compared with those without the allele.

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**(Choice E)** Islet amyloid polypeptide is a normal secretory product of pancreatic beta cells that forms cytotoxic deposits in type 2 diabetes mellitus, impairing beta-cell function.

**Educational objective:**

Patients with trisomy 21 (Down syndrome) have 3 copies of the amyloid precursor protein gene located on chromosome 21. This increases amyloid-beta accumulation in the brain, placing these patients at high risk for developing early-onset Alzheimer disease.

**References**

- Aging in Down syndrome and the development of Alzheimer's disease neuropathology.

Genetics Nervous System Down syndrome



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A 35-year-old woman, gravida 2 para 1, comes to the office for a routine prenatal visit. Her first child was born with a hydrocele and syndactyly of the first and second toes. The patient has no significant medical problems and takes no medications except for a multivitamin. Examination reveals clear lungs and normal first and second heart sounds. The abdomen is soft and nontender. Uterine size, fetal movements, and fetal cardiac activity are all within appropriate limits. The patient undergoes amniocentesis during the 18th week of pregnancy. Amniotic fluid analysis shows an increased level of acetylcholinesterase. This patient's amniocentesis results most likely suggest failure of which of the following processes?

A. Epithelial cell apoptosis in the embryonic duodenum
B. Fusion of the edges of the neural plate
C. Involution of the thyroglossal duct
D. Meiotic disjunction of chromosome 21
E. Migration of neural crest cells
F. Obliteration of the processus vaginalis



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born with a hydrocele and syndactyly of the first and second toes. The patient has no significant medical problems and takes no medications except for a multivitamin. Examination reveals clear lungs and normal first and second heart sounds. The abdomen is soft and nontender. Uterine size, fetal movements, and fetal cardiac activity are all within appropriate limits. The patient undergoes amniocentesis during the 18th week of pregnancy. Amniotic fluid analysis shows an increased level of acetylcholinesterase. This patient's amniocentesis results most likely suggest failure of which of the following processes?

A. ~~Epithelial cell apoptosis in the embryonic duodenum~~ (5%)

✓ B. Fusion of the edges of the neural plate (57%)

C. ~~Involution of the thyroglossal duct~~ (2%)

D. ~~Meiotic disjunction of chromosome 21~~ (13%)

E. ~~Migration of neural crest cells~~ (16%)

F. ~~Obliteration of the processus vaginalis~~ (3%)

Correct

57%

33 secs

10/28/2020



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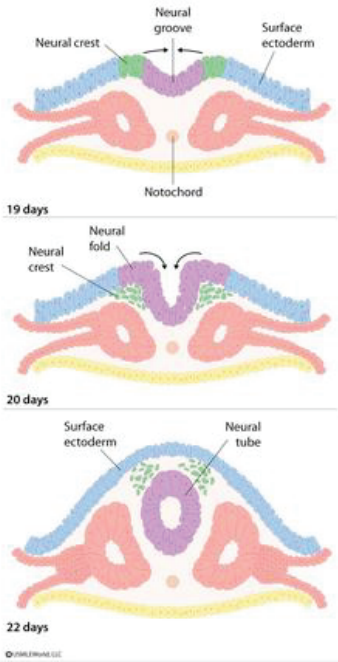
## Exhibit Display

Neural tube formation

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**Neural tube defects** (NTDs) occur due to **failure of fusion** of the neural plate edges during the 4th week of fetal development. Fusion begins in the cervical region and proceeds toward the cranial and caudal ends of the neural tube (ie, the rostral and caudal neuropores). Failure of the rostral neuropore to close results in **anencephaly**, whereas impaired closure of the caudal neuropore causes spina bifida. If either neuropore does not fuse, an opening persists between the neural tube and the amniotic cavity that allows leakage of **alpha-fetoprotein** (AFP) and **acetylcholinesterase** (AChE) into the amniotic fluid. AFP can also cross the placenta and is detectable in the maternal serum. Detection of AFP and AChE is used for prenatal screening of NTDs (eg, spina bifida cystica, anencephaly).

**(Choice A)** Duodenal atresia is a result of impaired recanalization of the duodenal lumen due to failure of epithelial cell apoptosis during fetal life. Although it can cause increased levels of amniotic fluid (ie, polyhydramnios), it is not associated with elevated levels of AChE. The first child's syndactyly is also an example of failed apoptosis of mesenchyme between the digits.

**(Choice C)** Failed involution of the thyroglossal tract can lead to formation of a persistent thyroglossal duct cyst. It typically presents as a painless midline mass close to the body of the hyoid bone. Amnionic fluid AChE level is not elevated.



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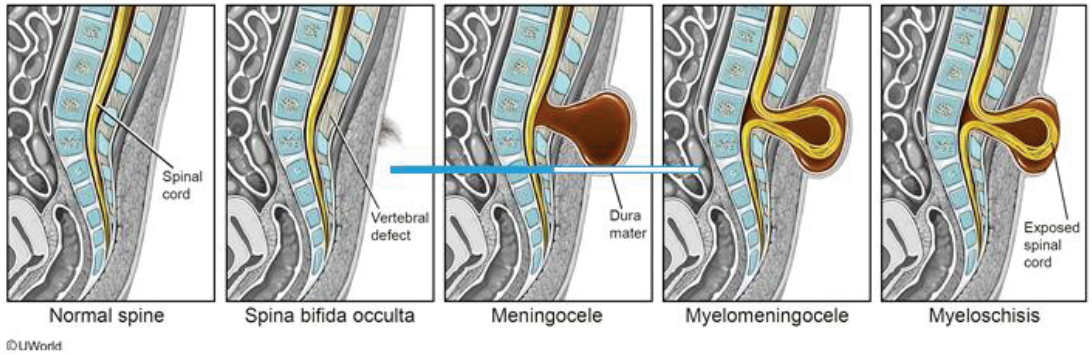


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AChE level is not elevated.

**(Choice D)** Chromosomal disjunction during meiosis involves separation of 23 pairs of homologous chromosomes in anaphase I, followed by separation of 23 pairs of sister chromatids during anaphase II. Advanced maternal age is a risk factor for Down syndrome (nondisjunction of chromosome 21), which presents with low AFP and normal AChE levels in the amniotic fluid.

**(Choice E)** Hirschsprung disease involves failure of neural crest cells to migrate into the sigmoid colon/rectum. It leads to absence of the myenteric and submucosal nervous plexuses, causing tonic constriction of the affected intestinal segments with consequent bilious emesis, abdominal distension, and failure to pass meconium.

**(Choice F)** Failure of the processus vaginalis to obliterate can lead to congenital hydrocele or indirect inguinal hernia. Neither condition is associated with increased amniotic AChE levels.

**Educational objective:**
Neural tube defects most often occur when the neural folds fail to fuse in the region of the anterior or posterior neuropores. Persistent communication between the spinal canal and the amniotic cavity allows leakage of alpha-fetoprotein (AFP) and acetylcholinesterase (AChE) into the amnionic fluid, leading to elevated levels of AFP and AChE that can be detected on amniocentesis.


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AChE level is not elevated.

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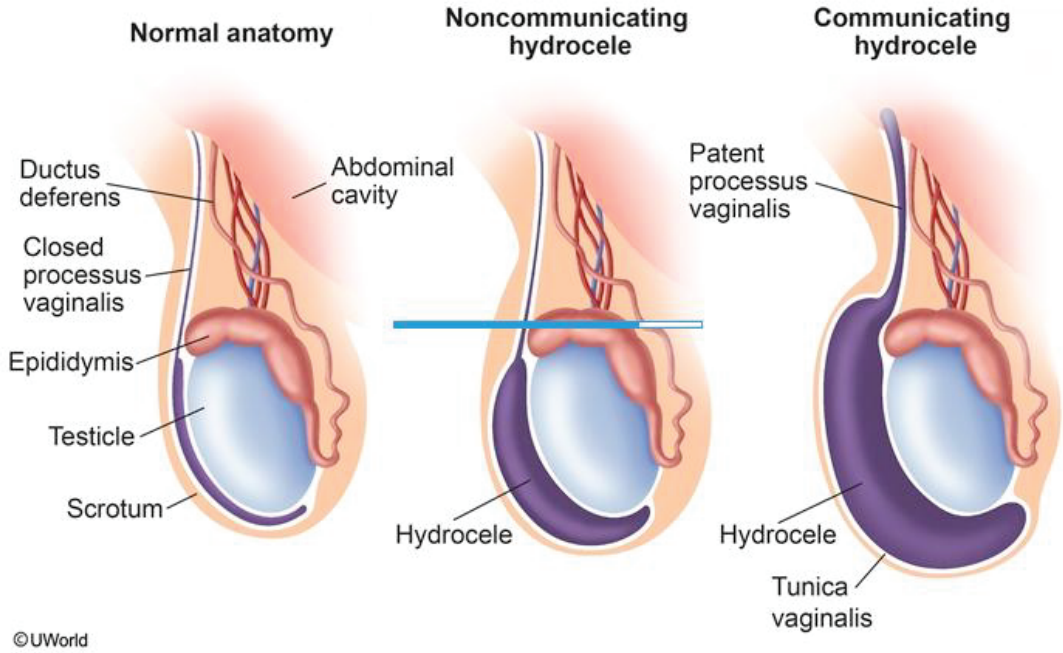


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AChE level is not elevated.

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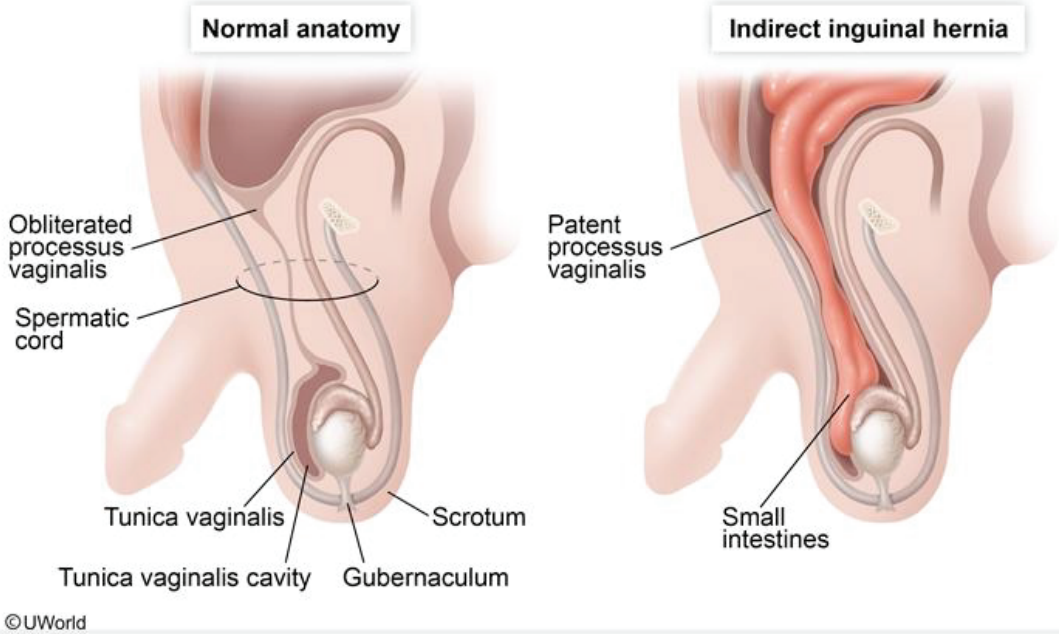
## Indirect inguinal hernia

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An 8-month-old girl is brought to the office for evaluation of irritability and regression of motor skills. Her birth was unremarkable and she appeared to develop normally, but she can no longer sit or roll over. Her parents have also noticed that she startles easily with loud noises. Head circumference measurement is consistent with macrocephaly. Bilateral funduscopic evaluation shows a bright red fovea centralis that is surrounded by a contrasting white macula. Peripheral vision is decreased. Abdominal examination is normal. Accumulation of which of the following metabolites is most likely present in this patient's tissues?

A. Galactocerebroside
B. Globotriaosylceramide
C. Glucocerebroside
D. Glycogen
E. $GM_2$ ganglioside
F. Heparan sulfate
G. Sphingomyelin



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birth was unremarkable and she appeared to develop normally, but she can no longer sit or roll over. Her parents have also noticed that she startles easily with loud noises. Head circumference measurement is consistent with macrocephaly. Bilateral funduscopic evaluation shows a bright red fovea centralis that is surrounded by a contrasting white macula. Peripheral vision is decreased. Abdominal examination is normal. Accumulation of which of the following metabolites is most likely present in this patient's tissues?

- A. Galactocerebroside (11%)
- B. Globotriaosylceramide (1%)
- C. Glucocerebroside (9%)
- D. Glycogen (1%)
- ✓ E. $GM_2$ ganglioside (56%)
- F. Heparan sulfate (2%)
- G. Sphingomyelin (17%)

Correct

56%

01 min, 49 secs

02/13/2021



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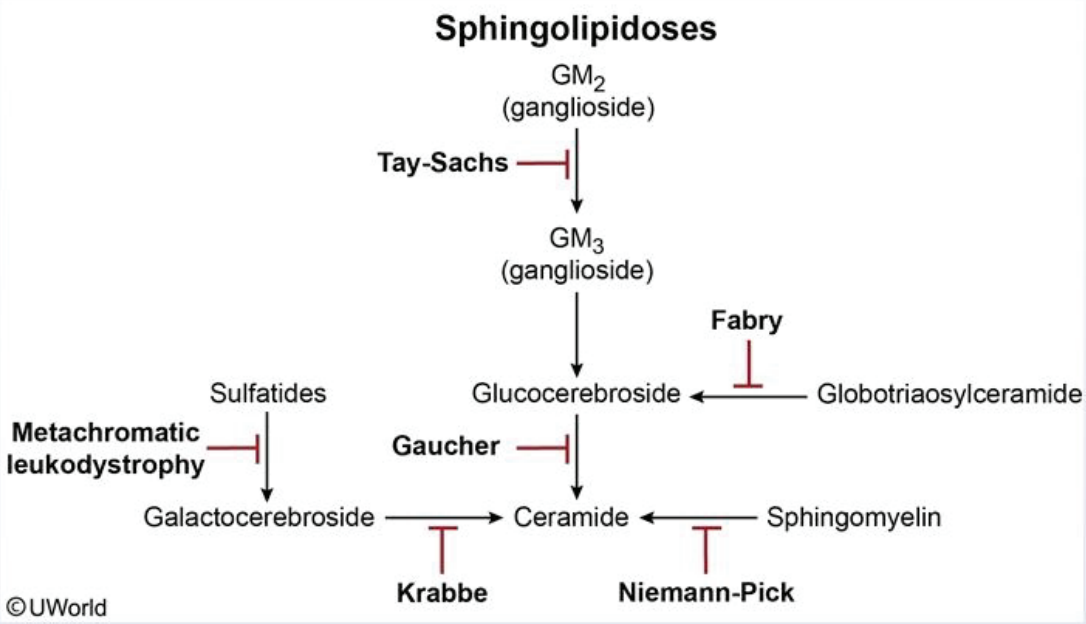


Tay-Sachs disease is an autosomal recessive neurodegenerative disorder commonly seen in the Ashkenazi Jewish population. Tay-Sachs is caused by β-hexosaminidase A deficiency, which results in accumulation of the cell membrane glycolipid **GM2 ganglioside** within lysosomes.


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Affected infants typically have normal development in the first few months of life, followed by progressive **neurologic deterioration** as glycolipids accumulate in the brain. Clinical consequences include weakness, hypotonia, developmental regression, seizures, blindness, and spasticity. Physical examination shows macrocephaly and an abnormal startle reflex with acoustic stimuli. In addition, the center of the fovea (blue arrow) appears bright red (**cherry-red macula spot**) as it is surrounded by white macula appearing as a halo. The halo results from a loss of retinal transparency due to ganglioside buildup in ganglion cells. The center of the fovea lacks ganglion cells, so the underlying choroid transmits its red color. Patients usually die by age 2-5 years.

**(Choice A)** Like Tay Sachs, Krabbe disease (galactocerebroside accumulation) causes progressive neurodegeneration. However, patients with Krabbe disease also have peripheral neuropathy and optic atrophy.

**(Choice B)** Fabry disease (globotriaosylceramide accumulation) causes angiokeratomas, peripheral neuropathy, and glomerulopathy that typically present in adulthood.

**(Choices C and G)** A similar cherry-red spot occurs in other lysosomal enzyme deficiencies, such as Gaucher disease and Niemann-Pick disease. Gaucher disease (β-glucocerebroside accumulation) and Niemann-Pick disease (sphingomyelin accumulation) are both unlikely due to this patient's normal


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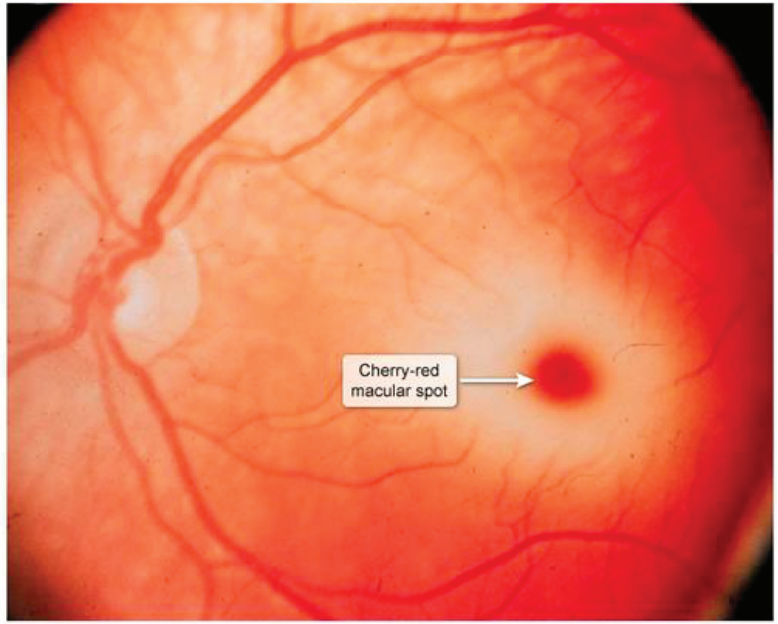
## Exhibit Display

**Cherry-red macular spot**

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Niemann-Pick disease (sphingomyelin accumulation) are both unlikely due to this patient's normal



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**(Choices C and G)** A similar cherry-red spot occurs in other lysosomal enzyme deficiencies, such as Gaucher disease and Niemann-Pick disease. Gaucher disease (β-glucocerebroside accumulation) and Niemann-Pick disease (sphingomyelin accumulation) are both unlikely due to this patient's normal abdominal examination (eg, no hepatosplenomegaly).

**(Choice D)** Glycogen storage diseases include von Gierke disease and Pompe disease. Infants with von Gierke disease (glucose-6-phosphatase deficiency) typically have hepatomegaly, hypoglycemia, seizures, and/or lactic acidosis. Pompe disease (lysosomal α-1,4-glucosidase deficiency) classically causes cardiomegaly and severe hypotonia.

**(Choice F)** Mucopolysaccharidosis (eg, Hurler syndrome, Hunter syndrome) are lysosomal storage disorders that cause buildup of glycosaminoglycans (GAGs) such as heparan and dermatan sulfate. GAG accumulation causes neurocognitive decline as well as coarse facial features and skeletal abnormalities.

**Educational objective:**

Tay-Sachs disease is an autosomal recessive disorder caused by β-hexosaminidase A deficiency, which results in $GM_2$ ganglioside accumulation. Key clinical features include progressive neurodegeneration and a cherry-red macular spot. In contrast to patients with Niemann-Pick disease, those with Tay Sachs disease have no hepatosplenomegaly.


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A 61-year-old man is brought to the emergency department after being found unresponsive on a sidewalk. Paramedics notice that the patient's breath smells of alcohol and that he has vomitus in his mouth. The patient also has agonal respirations, and cardiac monitoring shows pulseless electrical activity. Resuscitation efforts are unsuccessful, and he is pronounced dead on arrival. Autopsy reveals that the cause of death is airway occlusion by aspirated vomitus. In addition, foci of hemorrhage and necrosis are seen in the mammillary bodies and gray matter surrounding the third and fourth ventricles. This patient's brain findings are most likely associated with a decrease in which of the following?

A. Blood protoporphyrin level
B. Erythrocyte glucose-6-phosphate dehydrogenase activity
C. Erythrocyte glutathione reductase activity
D. Erythrocyte transketolase activity
E. Serum methylmalonic acid level
F. Serum NADPH level



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Paramedics notice that the patient's breath smells of alcohol and that he has vomitus in his mouth. The patient also has agonal respirations, and cardiac monitoring shows pulseless electrical activity. Resuscitation efforts are unsuccessful, and he is pronounced dead on arrival. Autopsy reveals that the cause of death is airway occlusion by aspirated vomitus. In addition, foci of hemorrhage and necrosis are seen in the mammillary bodies and gray matter surrounding the third and fourth ventricles. This patient's brain findings are most likely associated with a decrease in which of the following?

A. ~~Blood protoporphyrin level~~ (2%)
B. Erythrocyte glucose-6-phosphate dehydrogenase activity (7%)
C. Erythrocyte glutathione reductase activity (12%)
D. Erythrocyte transketolase activity (48%)
E. ~~Serum methylmalonic acid level~~ (11%)
F. ~~Serum NADPH level~~ (17%)

Correct

48%
02 mins, 58 secs
10/24/2020



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**Wernicke encephalopathy** classically presents with the triad of ophthalmoplegia, ataxia, and confusion, and can lead to coma and death if left untreated. Foci of **hemorrhage and necrosis** in the **mammillary bodies** and periaqueductal gray matter are typically found on autopsy. This condition occurs due to chronic thiamine deficiency, which is common in patients with **alcoholism**.

Thiamine (vitamin $B_1$) participates in glucose metabolism and is a cofactor for the following enzymes:

1. Pyruvate dehydrogenase, which converts pyruvate (glycolysis end product) into acetyl-CoA (enters the citric acid cycle)
2. α-Ketoglutarate dehydrogenase, an enzyme of the citric acid cycle
3. Branched-chain α-ketoacid dehydrogenase, which is essential for catabolism of branched-chain amino acids (eg, leucine, isoleucine, valine)
4. Transketolase, an enzyme of the pentose phosphate pathway that helps convert ribulose 5-P (derived from glucose) to glycolysis intermediates (eg, glyceraldehyde 3-P)

**Thiamine deficiency**, therefore, results in decreased glucose utilization, which is especially pronounced in the central nervous system. If a patient with chronic thiamine deficiency is given a glucose infusion without thiamine supplementation, acute cerebral damage may occur. Thiamine deficiency can be diagnosed if baseline **erythrocyte transketolase activity** is low but increases after addition of thiamine



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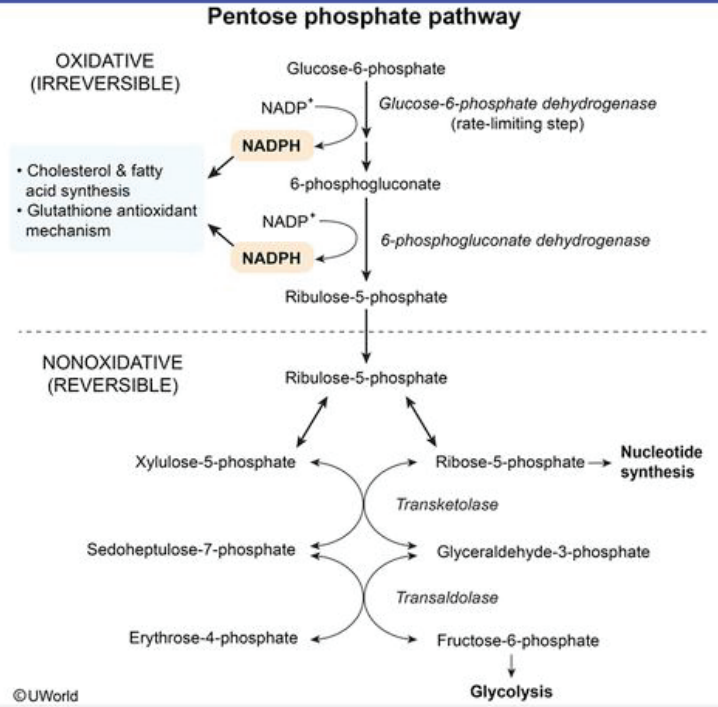


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baseline **erythrocyte transketolase activity** is low but increases after addition of thiamine



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from glucose) to glycolysis intermediates (eg, glyceraldehyde 3-P)

**Thiamine deficiency**, therefore, results in decreased glucose utilization, which is especially pronounced in the central nervous system. If a patient with chronic thiamine deficiency is given a glucose infusion without thiamine supplementation, acute cerebral damage may occur. Thiamine deficiency can be diagnosed if baseline **erythrocyte transketolase activity** is low but increases after addition of thiamine pyrophosphate. In actual practice, if a patient is suspected of alcoholism or malnutrition, thiamine deficiency should be presumed and he or she should receive thiamine supplementation with glucose infusion.

**(Choice A)** Protoporphyrin is a precursor of heme. Increased erythrocyte protoporphyrin concentration is the hallmark of erythropoietic protoporphyria; however, this elevation is nonspecific and can be seen in other conditions (eg, iron deficiency anemia, lead poisoning).

**(Choice B)** Erythrocyte glucose-6-phosphate dehydrogenase (G6PD) catalyzes the rate-limiting step in the pentose phosphate pathway, which is necessary for production of NADPH and proper functioning of the erythrocyte antioxidant system. Decreased G6PD levels cause hemolytic anemia.

**(Choices C and F)** NADH and NADPH are both derived from niacin (vitamin $B_3$). NADPH is a cofactor for glutathione reductase, an enzyme that helps metabolize harmful reactive oxygen species. Neither NADPH


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other conditions (eg, iron deficiency anemia, lead poisoning).

**(Choice B)** Erythrocyte glucose-6-phosphate dehydrogenase (G6PD) catalyzes the rate-limiting step in the pentose phosphate pathway, which is necessary for production of NADPH and proper functioning of the erythrocyte antioxidant system. Decreased G6PD levels cause hemolytic anemia.

**(Choices C and F)** NADH and NADPH are both derived from niacin (vitamin $B_3$). NADPH is a cofactor for glutathione reductase, an enzyme that helps metabolize harmful reactive oxygen species. Neither NADPH nor erythrocyte glutathione reductase is used for diagnosing thiamine deficiency.

**(Choice E)** Methylmalonic acid, a product of fatty acid oxidation, is converted to succinyl-CoA by the enzyme methylmalonyl-CoA mutase (uses vitamin $B_{12}$ as a cofactor). Consequently, methylmalonic acid levels are increased in vitamin $B_{12}$ deficiency.

**Educational objective:**
Chronic thiamine (vitamin $B_1$) deficiency impairs glucose utilization in the central nervous system. This occurs due to decreased activity of the enzymes that use thiamine as a cofactor (eg, pyruvate dehydrogenase, α-ketoglutarate dehydrogenase, transketolase). Thiamine deficiency can be diagnosed if baseline erythrocyte transketolase activity is low but increases after addition of thiamine pyrophosphate.



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A 34-year-old man comes to the hospital due to several hours of difficulty swallowing, dry mouth, and blurred vision. The patient has a history of major depression. Examination shows mydriasis and poorly reactive pupils. Electrodiagnostic studies reveal normal nerve conduction velocity but decreased compound muscle action potential (CMAP). Rapid, repetitive nerve stimulation leads to facilitation of CMAP. Further review of this patient's medical history would most likely reveal which of the following?

A. Consumption of home-canned food
B. Diarrheal disease after eating undercooked poultry
C. Episodic diplopia and ptosis
D. Occupational exposure to insecticides
E. Recent consumption of puffer fish
F. Tricyclic antidepressant overdose

Submit



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A 34-year-old man comes to the hospital due to several hours of difficulty swallowing, dry mouth, and blurred vision. The patient has a history of major depression. Examination shows mydriasis and poorly reactive pupils. Electrodiagnostic studies reveal normal nerve conduction velocity but decreased compound muscle action potential (CMAP). Rapid, repetitive nerve stimulation leads to facilitation of CMAP. Further review of this patient's medical history would most likely reveal which of the following?

- A. Consumption of home-canned food (33%)
- B. ~~Diarrheal disease after eating undercooked poultry~~ (2%)
- C. ~~Episodic diplopia and ptosis~~ (6%)
- D. ~~Occupational exposure to insecticides~~ (11%)
- E. ~~Recent consumption of puffer fish~~ (8%)
- F. Tricyclic antidepressant overdose (37%)

Incorrect
Correct answer

33%
Answered correctly

01 min, 27 secs
Time Spent

10/13/2020
Last Updated



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The combination of **nicotinic** (eg, diplopia, dysphagia) and **muscarinic blockade** (eg, dry mouth) is strongly suggestive of food poisoning with ***Clostridium botulinum* toxin**, a highly potent preformed neurotoxin. The toxin **inhibits acetylcholine release** from presynaptic nerve terminals at the neuromuscular junction (NMJ), thereby preventing muscular contraction. This effect can be seen on electromyography as a decrease in the compound muscle action potential (CMAP, or electrical response of the muscle) following stimulation of a motor nerve. High-rate, repetitive nerve stimulation improves the deficit as the rapid depolarization rate increases calcium concentration in the presynaptic nerve terminal, helping mobilize additional acetylcholine vesicles.

The anaerobic environment within **canned foods** contaminated by *C botulinum* spores allows for germination and growth of the organism. The toxin (produced by vegetative bacteria) is **not** actively secreted, remaining intracellular until autolysis causes its release into food. The toxin is readily destroyed by heat; however, if food containing the toxin is not cooked properly, the classic **diplopia, dysphagia, and dysphonia ("3 Ds")** can develop within 12-36 hours of consumption.

**(Choice B)** Guillain-Barré syndrome can develop following *Campylobacter jejuni* infection and is characterized by absent reflexes and progressive symmetric weakness, typically starting from the lower extremities (unlike botulism, which commonly causes descending paralysis starting from the cranial



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characterized by absent reflexes and progressive symmetric weakness, typically starting from the lower extremities (unlike botulism, which commonly causes descending paralysis starting from the cranial nerves).

**(Choice C)** Myasthenia gravis (autoimmune attack against postsynaptic nicotinic receptors) is characterized by episodic diplopia and ptosis. However, muscarinic symptoms (eg, dry mouth, mydriasis) are not characteristic, and CMAP does not improve with rapid, repetitive nerve stimulation. In contrast, Lambert-Eaton syndrome (autoantibodies against presynaptic voltage-gated calcium channels) can present with muscarinic symptoms and improved CMAP with rapid nerve stimulation, but the initial weakness typically involves the proximal extremities (particularly legs).

**(Choice D)** Poisoning due to organophosphates (acetylcholinesterase inhibitors) used in insecticides reflects depolarizing blockade (muscle weakness, fasciculations, paralysis), central nervous system effects (lethargy, seizures), and muscarinic overstimulation (miosis, bradycardia, increased lacrimation and salivation).

**(Choice E)** Tetrodotoxin poisoning (due to contaminated puffer fish ingestion) leads to inhibition of sodium influx into nerve cells. Manifestations include weakness, paresthesias (face, extremities), loss of reflexes, and sometimes severe hypotension. Patients commonly remain conscious, although paralyzed.



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(lethargy, seizures), and muscarinic overstimulation (miosis, bradycardia, increased lacrimation and salivation).

**(Choice E)** Tetrodotoxin poisoning (due to contaminated puffer fish ingestion) leads to inhibition of sodium influx into nerve cells. Manifestations include weakness, paresthesias (face, extremities), loss of reflexes, and sometimes severe hypotension. Patients commonly remain conscious, although paralyzed.

**(Choice F)** Anticholinergic toxicity is one of the manifestations of tricyclic antidepressant overdose. However, this produces muscarinic (not nicotinic) blockade with no effect on the NMJ (ie, no alterations in CMAP).

**Educational objective:**

Botulinum neurotoxin produced by *Clostridium botulinum* prevents the release of acetylcholine from presynaptic nerve terminals. The toxin impairs peripheral muscarinic and nicotinic neurotransmission, causing both autonomic symptoms (eg, fixed pupillary dilation, dry mouth) and skeletal muscle weakness (eg, diplopia, dysphagia, respiratory depression). Its effects at the neuromuscular junction can be seen on electromyography as a decrease in muscle response following stimulation of a motor nerve.

| Microbiology | Nervous System | Botulism |
|---|---|---|
| Subject | System | Topic |



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A 54-year-old man is brought to the emergency department due to a week of progressive headaches and confusion. He was treated for viral esophagitis 6 months ago and *Pneumocystis* pneumonia 2 months ago. Temperature is 38 C (100.4 F), blood pressure is 142/86 mm Hg, and pulse is 64/min. The patient is lethargic and oriented to person and place only. CT scan of the head shows a mildly increased ventricle size but no other abnormalities. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein concentration and pleocytosis. The latex agglutination test is positive for soluble polysaccharide antigen. Light microscopy of this patient's cerebrospinal fluid is most likely to reveal which of the following?

A. Budding yeast
B. Germ tubes
C. Nonseptate hyphae
D. Spherules with endospores
E. Sporangium


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confusion. He was treated for viral esophagitis 6 months ago and *Pneumocystis* pneumonia 2 months ago. Temperature is 38 C (100.4 F), blood pressure is 142/86 mm Hg, and pulse is 64/min. The patient is lethargic and oriented to person and place only. CT scan of the head shows a mildly increased ventricle size but no other abnormalities. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein concentration and pleocytosis. The latex agglutination test is positive for soluble polysaccharide antigen. Light microscopy of this patient's cerebrospinal fluid is most likely to reveal which of the following?

- A. Budding yeast (50%)
- B. Germ tubes (6%)
- C. ~~Nonseptate hyphae~~ (9%)
- D. ~~Spherules with endospores~~ (21%)
- E. Sporangium (12%)

Correct

50%

03 mins, 05 secs

12/02/2020



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| *Cryptococcus neoformans* | |
|---|---|
| **Morphology** | • **Yeast** with a **polysaccharide capsule**<br>• Round/oval cells with narrow-based buds |
| **Epidemiology** | • Soil and pigeon droppings<br>• Respiratory transmission<br>• Opportunistic infection in patients with **AIDS** (CD4 <100/mm$^3$) |
| **Infection** | • **Meningoencephalitis:** Progressive headache, fever, confusion<br>• Possible disseminated disease |
| **Diagnosis** | • **India ink** stain of cerebrospinal fluid<br>• Latex agglutination of cerebrospinal fluid<br>• Culture using Sabouraud agar |
| **Treatment** | • **Amphotericin B** and flucytosine (induction)<br>• Fluconazole (maintenance) |



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| | |
|---|---|
| | • Culture using Sabouraud agar |
| **Treatment** | • **Amphotericin B** and flucytosine (induction)<br>• Fluconazole (maintenance) |

This patient's opportunistic infections (viral esophagitis, *Pneumocystosis* pneumonia) raise suspicion for **untreated AIDS**. He now has headache, fever, confusion, and polysaccharide antigens in the cerebrospinal fluid (CSF) indicating likely **cryptococcal meningitis**. This opportunistic infection is caused by *Cryptococcus neoformans*, a yeast with a thick **polysaccharide capsule**. Diagnosis is often made by identifying polysaccharide (cryptococcal) antigens in the CSF. Round or oval **budding yeast** can also be visualized with India ink stain. Most patients have **elevated opening pressures** on lumbar puncture due to increased vascular permeability secondary to inflammation and/or yeasts obstructing CSF outflow from the arachnoid villi.

**(Choice B)** *Candida albicans* forms germ tubes (true hyphae) if incubated in 37 C (98.6 F) serum for 3 hours. This test helps differentiate *C albicans* from other *Candida* species. *C albicans* meningitis is extremely rare (even in patients with HIV) and would not be associated with a positive polysaccharide antigen.

**(Choice C)** *Mucor* and *Rhizopus* species are characterized by nonseptate hyphae that branch at wide


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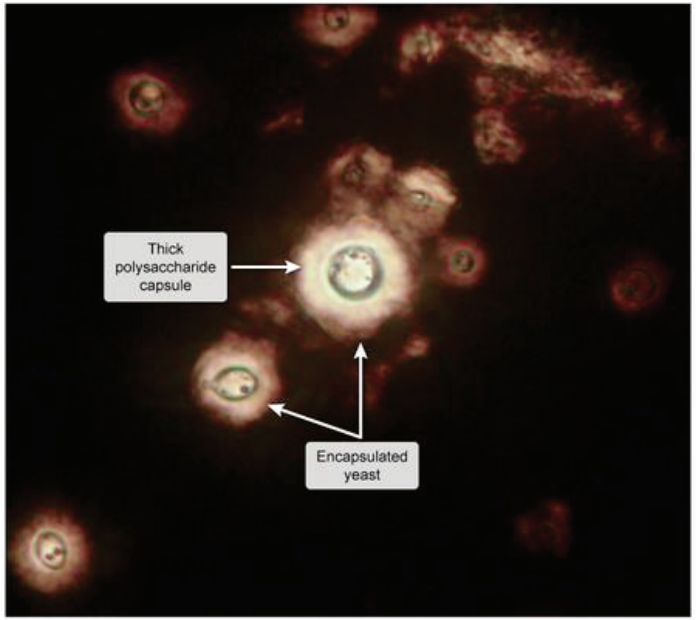
• Culture using Sabouraud agar

Exhibit Display

***Cryptococcus***




India ink stain

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(Choice C) Mucor and Rhizopus species are characterized by nonseptate hyphae that branch at wide



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**(Choice C)** *Mucor* and *Rhizopus* species are characterized by nonseptate hyphae that branch at wide angles. These fungi cause severe infections of the paranasal sinuses (mucormycosis) in patients who are immunosuppressed (eg, diabetes mellitus).

**(Choice D)** *Coccidioides immitis* is associated with the formation of spherules, which then rupture to release endospores. This fungus primarily causes community-acquired pneumonia in endemic areas (eg, Arizona desert); central nervous system infection is quite rare and would not be associated with a positive polysaccharide antigen.

**(Choice E)** Mold fungi (eg, *Rhizopus*) form sporangia, which produce and contain spores. *Cryptococcus* is a yeast and does not reproduce with sporangia.

**Educational objective:**
*Cryptococcus neoformans* causes meningoencephalitis in patients with untreated AIDS. Diagnosis can be made by detecting the polysaccharide capsule in cerebrospinal fluid using the latex agglutination test. India ink staining of cerebrospinal fluid is also used for diagnosis and can demonstrate round or oval budding yeast.

| Microbiology | Nervous System | Meningitis |
|---|---|---|
| Subject | System | Topic |


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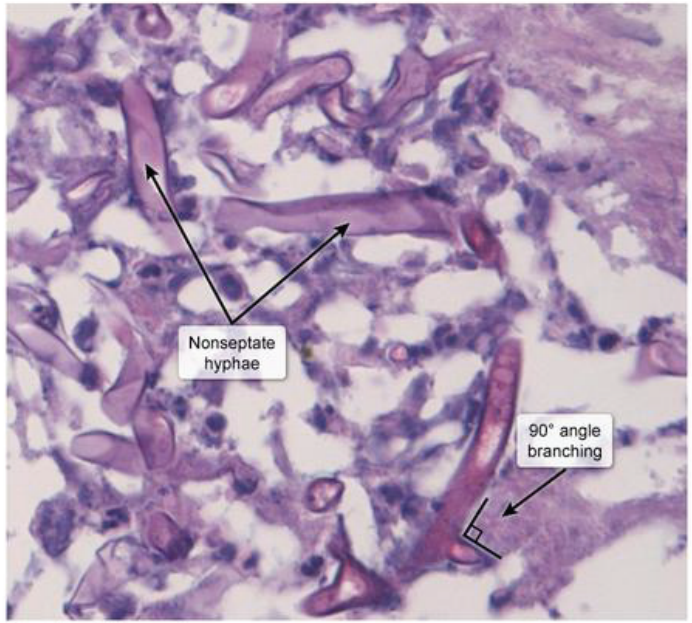
(Choice C) *Mucor* and *Rhizopus* species are characterized by nonseptate hyphae that branch at wide

Exhibit Display

Mucormycosis*




*Frequently due to *Rhizopus* or *Mucor*

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Subject System Topic



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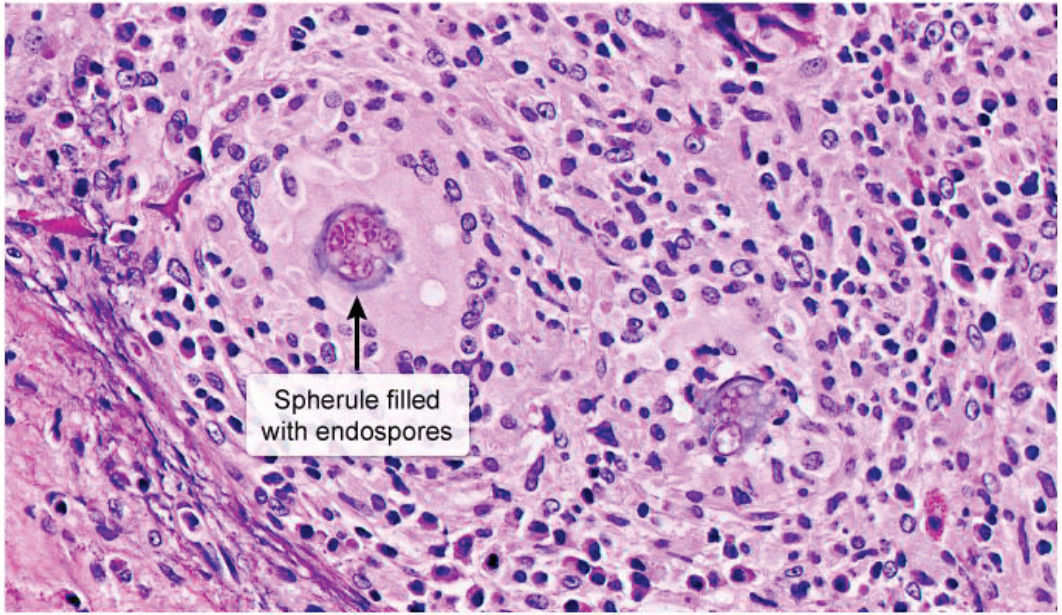
(Choice C) *Mucor* and *Rhizopus* species are characterized by nonseptate hyphae that branch at wide

Exhibit Display

***Coccidioides***

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A 48-year-old man comes to the hospital after a day of high-grade fever, progressive headache, and double vision. The patient has been having purulent nasal drainage and frontal headache for the past several days. He has a history of type 2 diabetes mellitus. His temperature is 38.9 C (102 F), blood pressure is 110/70 mm Hg, and pulse is 94/min. Physical examination shows ptosis, mydriasis, mild proptosis, and loss of the corneal reflex of the right eye. Visual acuity is normal in both eyes, but the patient is unable to move the right eye in any direction. There is decreased sensation in the right upper face. Which of the following structures is most likely involved in this patient's presentation?

A. Brainstem
B. Cavernous sinus
C. Frontal lobe of brain
D. Inferior orbital fissure
E. Jugular foramen
F. Optic chiasm



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A. Brainstem (7%)
B. Cavernous sinus (74%)
C. Frontal lobe of brain (2%)
D. Inferior orbital fissure (12%)
E. ~~Jugular foramen~~ (2%)
F. ~~Optic chiasm~~ (1%)

Incorrect
Correct answer

74%
01 min, 23 secs
11/10/2020



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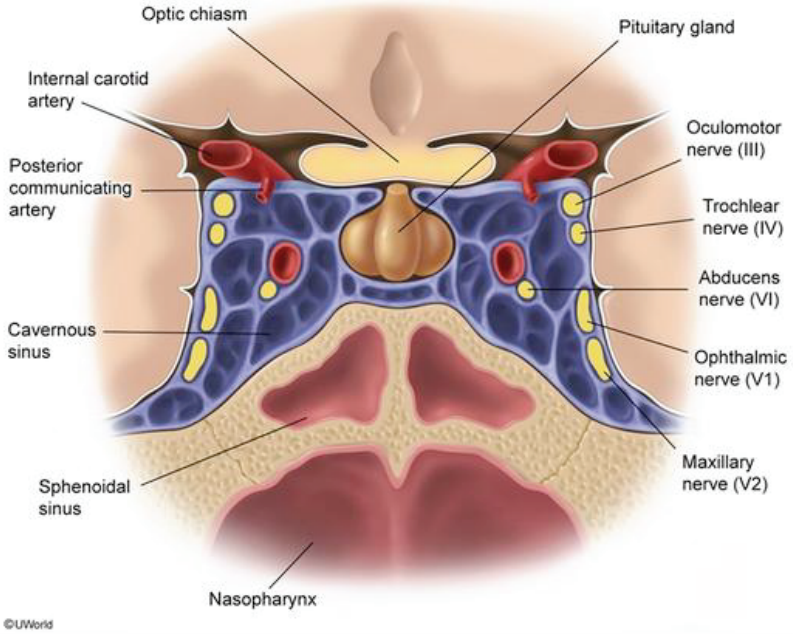
Exhibit Display

Cavernous sinus

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Nasopharynx

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**Cavernous sinus thrombosis** is most commonly due to contiguous spread of an infection from the medial third of the face, sinuses (ethmoidal or sphenoidal), or teeth. The infection can communicate in a retrograde fashion into the cavernous sinus through the valveless facial venous system (via the superior and inferior ophthalmic veins). Common pathogens include *Staphylococcus aureus* (most common) and streptococci, although fungal organisms (eg, *Mucor*, *Rhizopus*) are responsible in rare cases.

Patients typically experience headache, fever, and diplopia. Ocular muscle paralysis occurs due to injury of **cranial nerves (CNs) III, IV, and VI**. CN III palsy may also result in ptosis and mydriasis. Involvement of the ophthalmic and maxillary branches of **CN V** can cause loss of both upper facial sensation and the afferent limb of the corneal reflex. Proptosis (eye protrusion) and chemosis (conjunctival swelling) may also be evident due to impaired venous drainage through the ophthalmic veins.

**(Choice A)** Brainstem lesions typically result in crossed signs (ipsilateral cranial nerve palsies and contralateral hemiparesis), vertigo, and ataxia.

**(Choice C)** Frontal lobe pathology can cause disinhibition, problems with planning/organizing, and personality changes. CN deficits are not characteristic.

**(Choice D)** The inferior orbital fissure transmits the maxillary division of CN V, infraorbital vessels, and



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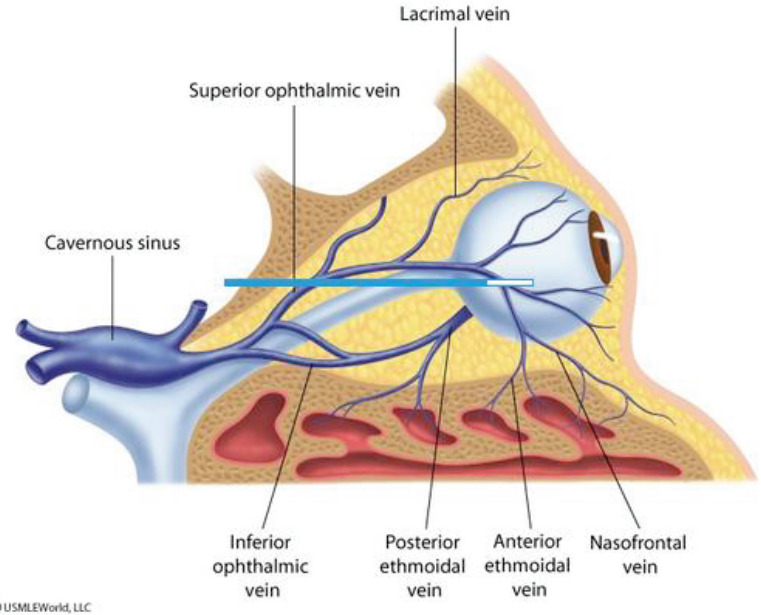
Nasopharynx

Exhibit Display

The valveless ophthalmic venous system

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(Choice D) The inferior orbital fissure transmits the maxillary division of CN V, infraorbital vessels, and



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**(Choice A)** Brainstem lesions typically result in crossed signs (ipsilateral cranial nerve palsies and contralateral hemiparesis), vertigo, and ataxia.

**(Choice C)** Frontal lobe pathology can cause disinhibition, problems with planning/organizing, and personality changes. CN deficits are not characteristic.

**(Choice D)** The inferior orbital fissure transmits the maxillary division of CN V, infraorbital vessels, and branches from the sphenopalatine ganglion.

**(Choice E)** Lesions of the jugular foramen can result in jugular foramen (Vernet) syndrome, which is characterized by the dysfunction of CNs IX, X, and XI. Findings include dysphagia, hoarseness, loss of gag reflex on the ipsilateral side, and deviation of the uvula toward the normal side.

**(Choice F)** The optic chiasm is superior to the cavernous sinus and is where the optic nerve fibers from the nasal side of each retina cross to the opposite side of the brain. Optic chiasm lesions typically cause bitemporal hemianopia, which is absent in this patient.

**Educational objective:**
Infection of the medial face, sinuses (ethmoidal or sphenoidal), or teeth may spread through the valveless facial venous system into the cavernous sinus, resulting in cavernous sinus thrombosis. Patients typically present with headache, fever, proptosis, and ipsilateral deficits in cranial nerves III, IV, VI, and V


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**(Choice D)** The inferior orbital fissure transmits the maxillary division of CN V, infraorbital vessels, and branches from the sphenopalatine ganglion.

**(Choice E)** Lesions of the jugular foramen can result in jugular foramen (Vernet) syndrome, which is characterized by the dysfunction of CNs IX, X, and XI. Findings include dysphagia, hoarseness, loss of gag reflex on the ipsilateral side, and deviation of the uvula toward the normal side.

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**Educational objective:**

Infection of the medial face, sinuses (ethmoidal or sphenoidal), or teeth may spread through the valveless facial venous system into the cavernous sinus, resulting in cavernous sinus thrombosis. Patients typically present with headache, fever, proptosis, and ipsilateral deficits in cranial nerves III, IV, VI, and V (ophthalmic and maxillary branches).

**References**

- Septic thrombosis of the cavernous sinuses.



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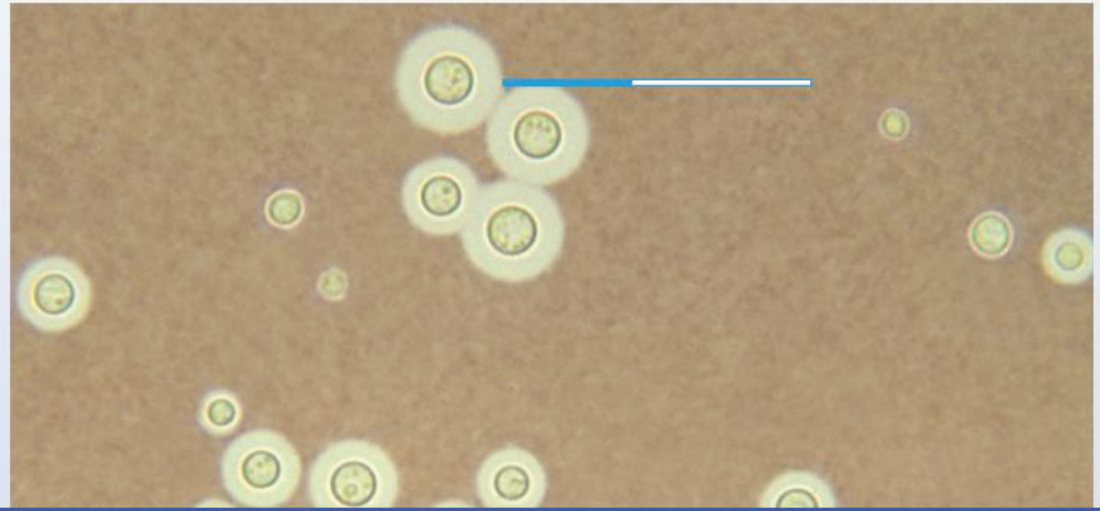
A 28-year-old man comes to the emergency department due to 2 weeks of headaches, fever, and episodes of inattentiveness. The patient has a history of Hodgkin lymphoma and is undergoing treatment with combination chemotherapy. Temperature is 38.2 C (100.8 F), blood pressure is 138/84 mm Hg, and pulse is 72/min. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein levels and low glucose levels. Light microscopy of the cerebrospinal fluid is shown in the image.





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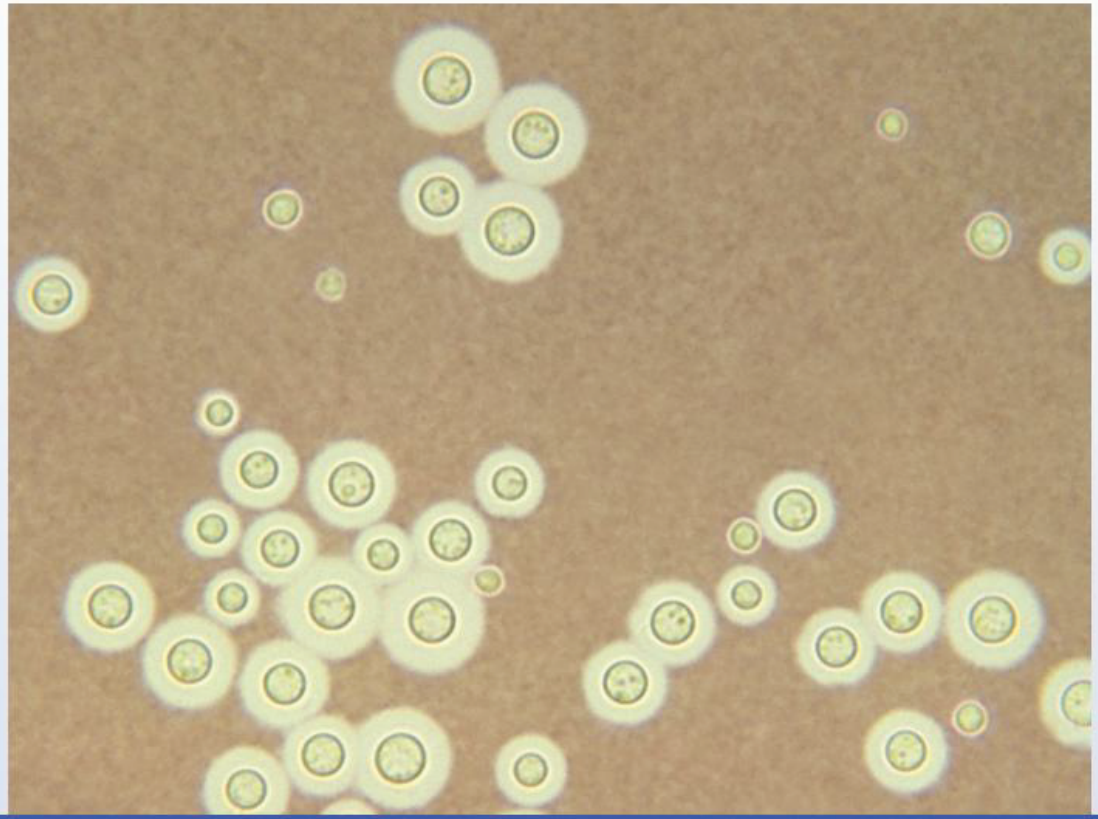
shown in the image.





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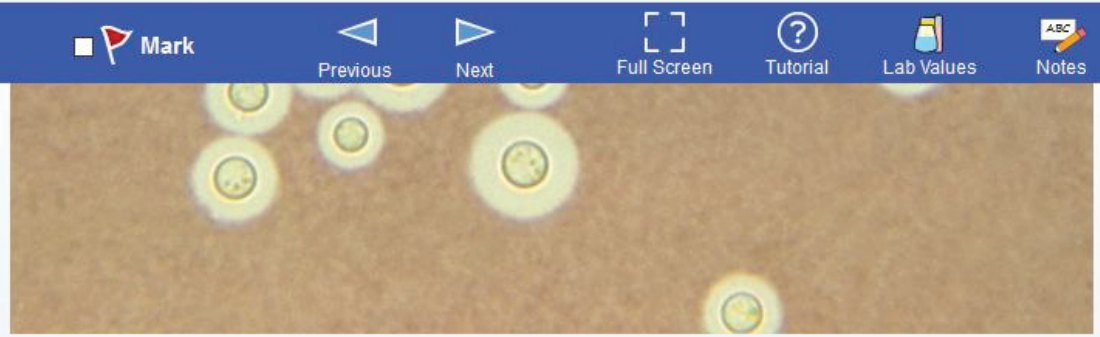

Which of the following should be included in initial treatment for this patient's current condition?

- A. Amphotericin B
- B. Ampicillin
- C. Ceftriaxone
- D. Ganciclovir
- E. Pyrimethamine
- F. Voriconazole

Submit



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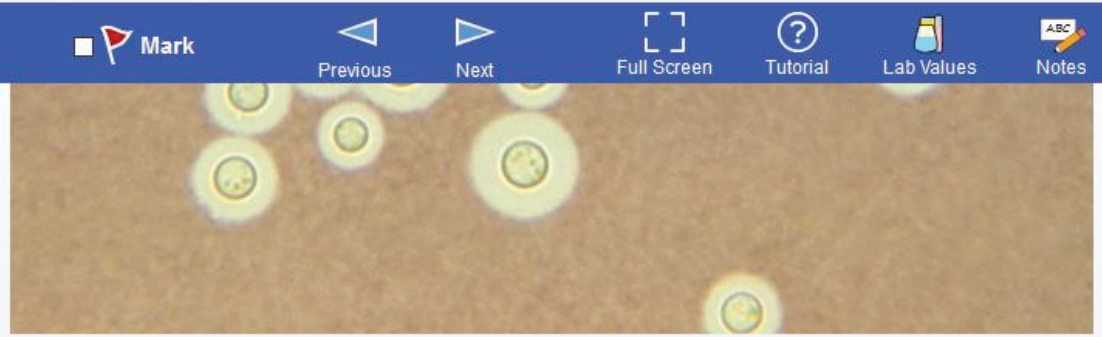

Which of the following should be included in initial treatment for this patient's current condition?

- A. Amphotericin B (82%)
- B. Ampicillin (1%)
- C. Ceftriaxone (5%)
- D. Ganciclovir (3%)
- E. Pyrimethamine (2%)
- F. Voriconazole (5%)



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| Clinical features of cryptococcal meningoencephalitis | |
|---|---|
| **Presentation** | • Headache, fever & lethargy typically developing over 2 weeks, sometimes longer<br>• Symptoms often more acute & severe in HIV patients |
| **Diagnosis** | • Lumbar puncture showing low glucose & increased protein; leukocyte count particularly low in HIV patients<br>• Transparent capsule seen on India ink staining<br>• Cryptococcal antigen detected in cerebrospinal fluid<br>• Culture on Sabouraud agar |
| **Treatment** | • Initial treatment: Amphotericin B & flucytosine<br>• Long-term maintenance therapy: Fluconazole |

***Cryptococcus neoformans*** is an opportunistic yeast that can be visualized with **India ink staining**. India ink stains the background of the slide black, which allows the **thick polysaccharide capsule** of the yeast to be visualized (clear halo between the dark background and the black center of the organism). India ink


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| | |
|---|---|
| Treatment | • Long-term maintenance therapy: Fluconazole |

***Cryptococcus neoformans*** is an opportunistic yeast that can be visualized with **India ink staining**. India ink stains the background of the slide black, which allows the **thick polysaccharide capsule** of the yeast to be visualized (clear halo between the dark background and the black center of the organism). India ink staining of the cerebrospinal fluid (CSF) is a common diagnostic modality in those with suspected cryptococcal meningitis. However, CSF cryptococcal (polysaccharide) antigen testing is more sensitive and specific, so it is also usually performed. Culture of the fungus on **Sabouraud agar** confirms the diagnosis.

Patients with cryptococcal meningitis usually develop slowly worsening headache, fever, and lethargy. Immunocompromised individuals are at greatest risk, particularly those who have AIDS or hematologic cancers or patients on chronic glucocorticoids. CSF analysis usually shows low glucose, increased protein, and mild pleocytosis with a predominance of lymphocytes. Initial treatment involves induction therapy with **amphotericin B** and flucytosine. Once patients are stabilized, they are switched to long-term maintenance therapy with fluconazole.

**(Choices B and C)** Ampicillin is used to treat *Listeria* meningitis; *Listeria* is a gram-positive rod with characteristic tumbling motility on light microscopy. Ceftriaxone can treat pneumococcal and *Haemophilus*


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characteristic tumbling motility on light microscopy. Ceftriaxone can treat pneumococcal and *Haemophilus influenzae* meningitis. Ampicillin and ceftriaxone are beta-lactam antibiotics that inhibit peptidoglycan cross-linking and lead to bactericidal effects. Fungi cannot be treated with beta-lactam antibiotics as their cell walls do not contain peptidoglycan.

**(Choice D)** Ganciclovir inhibits viral DNA synthesis and is used to treat cytomegalovirus meningoencephalitis, which is diagnosed using PCR.

**(Choice E)** Pyrimethamine is an antifolate agent used in the treatment of malaria and toxoplasmosis.

**(Choice F)** Azole drugs inhibit the synthesis of ergosterol, a crucial fungal cell membrane component. Spectrum of activity varies based on the particular agent; voriconazole is most effective against *Aspergillus*. Fluconazole is used for long-term maintenance therapy in cryptococcal meningitis, but is fungistatic at typically used doses and is less effective than amphotericin B for initial treatment.

**Educational objective:**
Patients with suspected cryptococcal meningitis can be diagnosed using India ink staining of the cerebrospinal fluid. Treatment with amphotericin B and flucytosine is required at first, followed by long-term fluconazole maintenance therapy.


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A 55-year-old man with poorly controlled hypertension and type 2 diabetes mellitus comes to the emergency department due to difficulty seeing. He has had blurry vision for the last 2 weeks, and 1 day ago he suddenly noticed a shadow develop across the visual field of his left eye. The patient has no recent headache, double vision, vertigo, light sensitivity, or nausea. On examination, pupils are equal and reactive to light. There is an area of reduced vision in the left eye. Funduscopic examination reveals a flame-shaped hemorrhage in the left temporal hemiretina. The transmission of visual information through which of the following neural structures will be disrupted?

A. Left inferior colliculus
B. Left lateral geniculate body
C. Left medial geniculate body
D. Medial optic chiasm
E. Right inferior colliculus
F. Right lateral geniculate body
G. Right medial geniculate body



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ago he suddenly noticed a shadow develop across the visual field of his left eye. The patient has no recent headache, double vision, vertigo, light sensitivity, or nausea. On examination, pupils are equal and reactive to light. There is an area of reduced vision in the left eye. Funduscopic examination reveals a flame-shaped hemorrhage in the left temporal hemiretina. The transmission of visual information through which of the following neural structures will be disrupted?

A. Left inferior colliculus (4%)
✓ B. Left lateral geniculate body (53%)
C. ~~Left medial geniculate body~~ (7%)
D. ~~Medial optic chiasm~~ (8%)
E. ~~Right inferior colliculus~~ (3%)
F. ~~Right lateral geniculate body~~ (18%)
G. ~~Right medial geniculate body~~ (5%)

Correct

53%
Answered correctly

03 mins, 33 secs
Time Spent

09/29/2020
Last Updated



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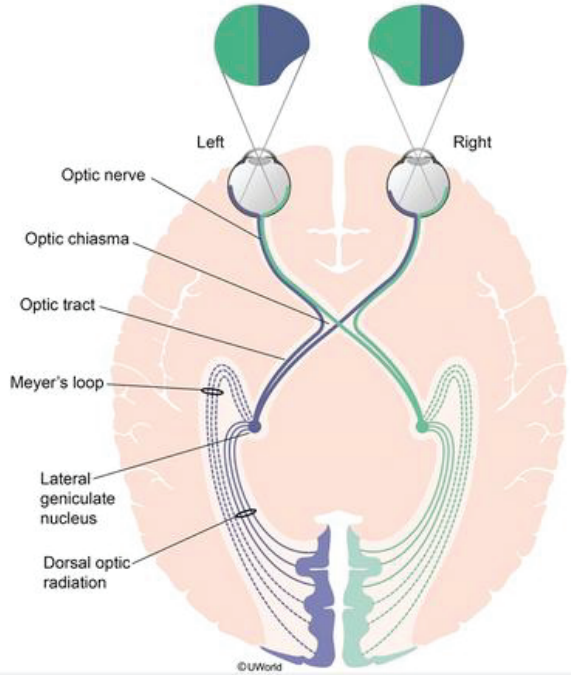
## Exhibit Display

**Visual pathways from above**

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This patient has a hypertensive hemorrhage in the left temporal hemiretina. The left temporal hemiretina receives visual information from the nasal visual field of the left eye. This **visual signal** is transmitted via the left optic nerve to the lateral aspect of the optic chiasm. It then joins the visual signal from the right nasal hemiretina (receives visual information from the temporal visual field of the right eye) and travels via the left optic tract to the left **lateral geniculate body** in the **thalamus**. After this homonymous visual signal leaves the left lateral geniculate body, it travels via the ipsilateral optic radiations to the ipsilateral primary visual cortex for visual processing.

**(Choices A, C, G and E)** The inferior colliculi and medial geniculate bodies are part of the auditory pathway.

**(Choice D)** The medial optic chiasm contains crossing nerve fibers that transmit visual information from the bilateral nasal hemiretinas.

**(Choice F)** The right lateral geniculate body receives visual information from the right temporal hemiretina and the left nasal hemiretina.

**Educational objective:**

Damage to the left temporal hemiretina will disrupt the transmission of visual information along the



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leaves the left lateral geniculate body, it travels via the ipsilateral optic radiations to the ipsilateral primary visual cortex for visual processing.

**(Choices A, C, G and E)** The inferior colliculi and medial geniculate bodies are part of the auditory pathway.

**(Choice D)** The medial optic chiasm contains crossing nerve fibers that transmit visual information from the bilateral nasal hemiretinas.

**(Choice F)** The right lateral geniculate body receives visual information from the right temporal hemiretina and the left nasal hemiretina.

**Educational objective:**
Damage to the left temporal hemiretina will disrupt the transmission of visual information along the ipsilateral optic nerve, lateral optic chiasm, optic tract, lateral geniculate body, optic radiations, and primary visual cortex.

**References**

- Anatomy of the visual pathways.



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A 15-year-old girl is evaluated for recurrent episodes of focal onset seizures evolving to bilateral tonic-clonic seizures over the past several months. She has also had headaches that are severe enough to keep her home from school. The patient has no prior medical conditions. MRI of the brain is shown in the exhibit. Which of the following histopathological findings are most likely present in the abnormal lesion?

A. Dense perivascular aggregates of atypical lymphoid cells

B. Infiltrating macrophages containing degraded myelin debris

C. Intense inflammatory infiltrate around *Toxoplasma* tachyzoites

D. Necrosis with surrounding pseudopalisading malignant cells

E. Tangle of large blood vessels with thickened walls

Submit



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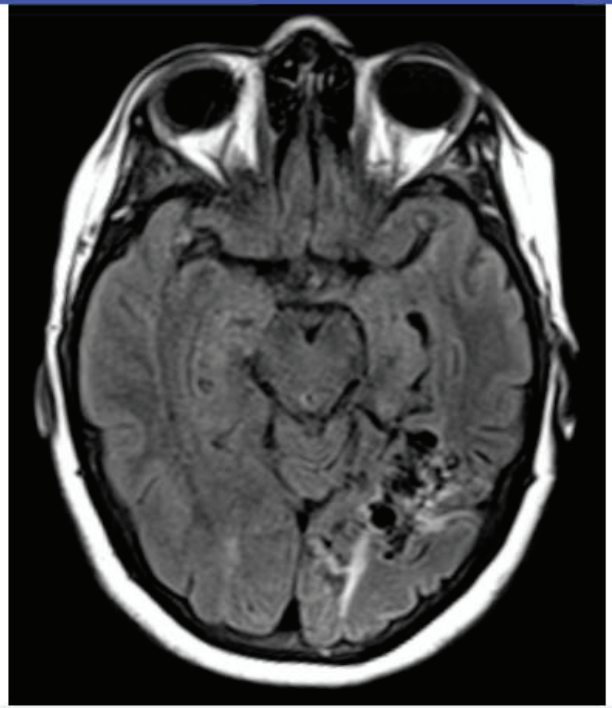
Exhibit Display



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A 15-year-old girl is evaluated for recurrent episodes of focal onset seizures evolving to bilateral tonic-clonic seizures over the past several months. She has also had headaches that are severe enough to keep her home from school. The patient has no prior medical conditions. MRI of the brain is shown in the exhibit. Which of the following histopathological findings are most likely present in the abnormal lesion?

A. Dense perivascular aggregates of atypical lymphoid cells (12%)

B. ~~Infiltrating macrophages containing degraded myelin debris~~ (15%)

C. ~~Intense inflammatory infiltrate around *Toxoplasma* tachyzoites~~ (8%)

D. ~~Necrosis with surrounding pseudopalisading malignant cells~~ (31%)

✓ E. Tangle of large blood vessels with thickened walls (32%)

Correct

32% Answered correctly

01 min, 23 secs Time Spent

03/07/2021 Last Updated

Explanation



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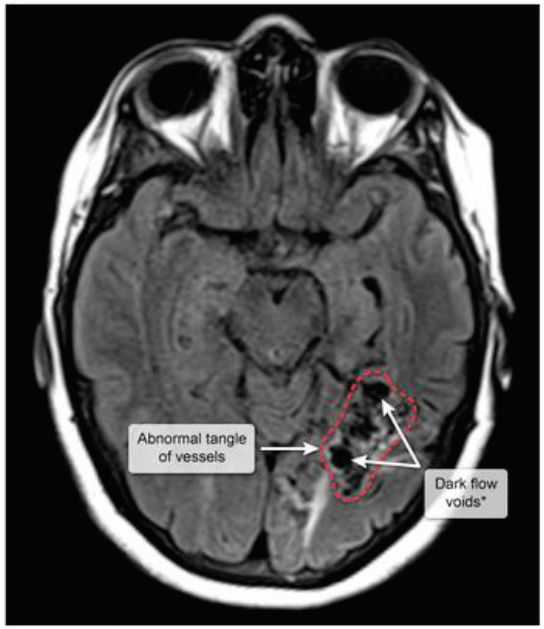
## Exhibit Display

**Cerebral arteriovenous malformation**

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Dark flow



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*Indicate swift blood flow

©UWorld

This patient with recurrent headaches and seizures has multiple flow voids in the left temporoparietal lobe demonstrated by MRI, consistent with a **cerebral arteriovenous malformation** (AVM).

AVMs are vascular malformations in which blood courses **directly from arteries to veins**, without passing through an intervening capillary bed. These tangled vessels with turbulent flow can lead to aneurysm development, bleeding, and damage to the surrounding brain. Microscopy of AVMs shows **abnormal vessels**, including irregular arteries and large veins with thickened walls, and gliotic brain tissue.

AVMs frequently present in children and young adults with **headaches** and **seizures** as well as **intracranial hemorrhage** (eg, intraparenchymal, subarachnoid hemorrhage). Some patients are initially asymptomatic and diagnosed incidentally by imaging. A nest of abnormal vessels with **"bag of worms"** appearance may be seen on angiography. MRI may reveal prior hemorrhage and multiple dark **flow voids**, indicative of swift blood flow.

**(Choice A)** Dense perivascular aggregates of atypical lymphoid cells are a histologic feature of primary CNS lymphoma, which is typically a diffuse large B-cell lymphoma. Although clinical symptoms may include seizures, it usually presents in older adults or immunocompromised patients. MRI would likely reveal an enhancing mass



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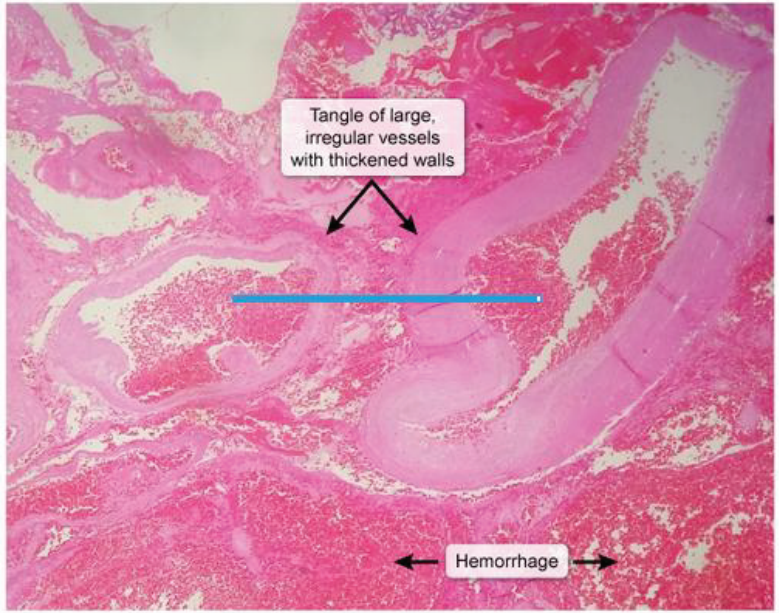
Exhibit Display

**Arteriovenous malformation**

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reveal an enhancing mass



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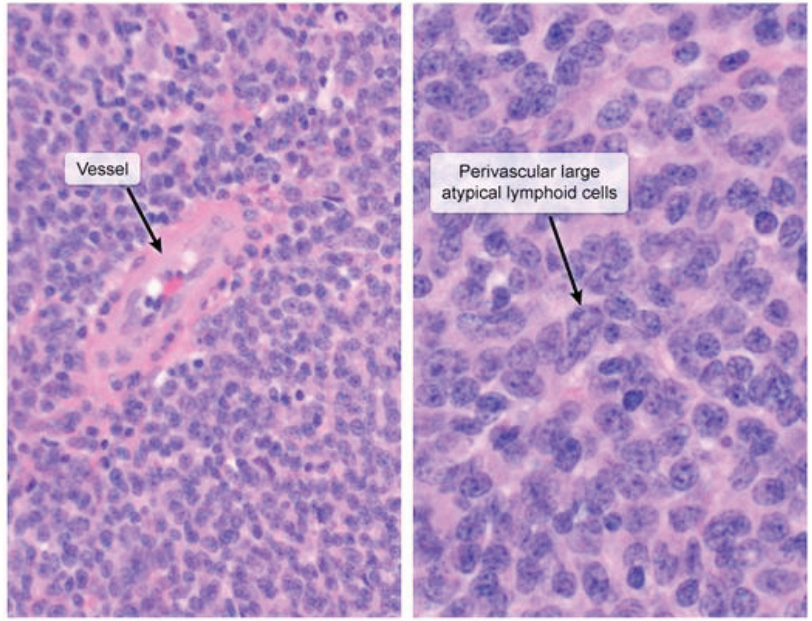
Exhibit Display

**Primary central nervous system lymphoma**

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reveal an enhancing mass



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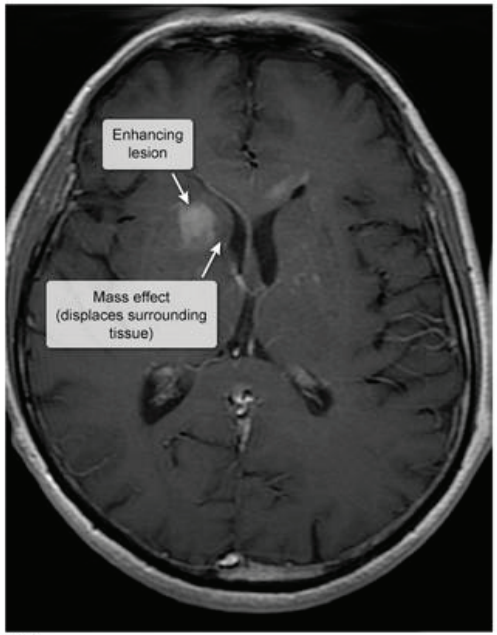
Exhibit Display

CNS lymphoma

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reveal an enhancing mass



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reveal an enhancing mass.

**(Choice B)** Lipid-laden macrophages with phagocytized myelin debris are seen in the demyelinating plaques of multiple sclerosis. Symptoms are variable but commonly include unilateral visual disturbance (eg, optic neuritis) and focal sensory and motor deficits. MRI typically reveals periventricular white matter lesions.

**(Choice C)** Histologic findings in cerebral *Toxoplasma gondii* infection include necrotic debris with surrounding inflammation, tachyzoites, and pseudocysts of bradyzoites. Although seizures and headaches are a frequent manifestation, CNS toxoplasmosis usually occurs in immunocompromised patients. Imaging would likely reveal ring-enhancing lesions.

**(Choice D)** Necrosis surrounded by malignant cells (pseudopalisading necrosis) and microvascular proliferation are features of glioblastoma, a high-grade infiltrating astrocytoma. It commonly presents with seizures, headache, and neurologic deficits in middle-aged or older adults (rather than children). MRI would likely reveal a mass with central hemorrhagic necrosis, vasogenic edema, and possible extension to the contralateral hemisphere.

**Educational objective:**

Cerebral arteriovenous malformations (AVMs) are vascular malformations histologically characterized by a


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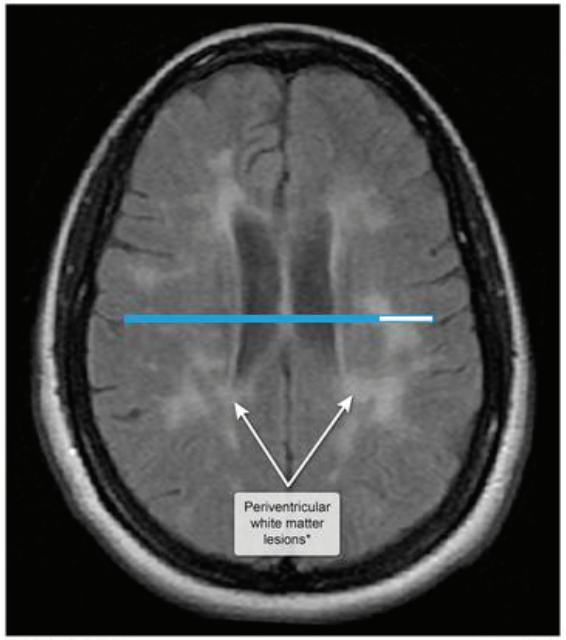
Exhibit Display

Multiple sclerosis

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Cerebral arteriovenous malformations (AVMs) are vascular malformations histologically characterized by a



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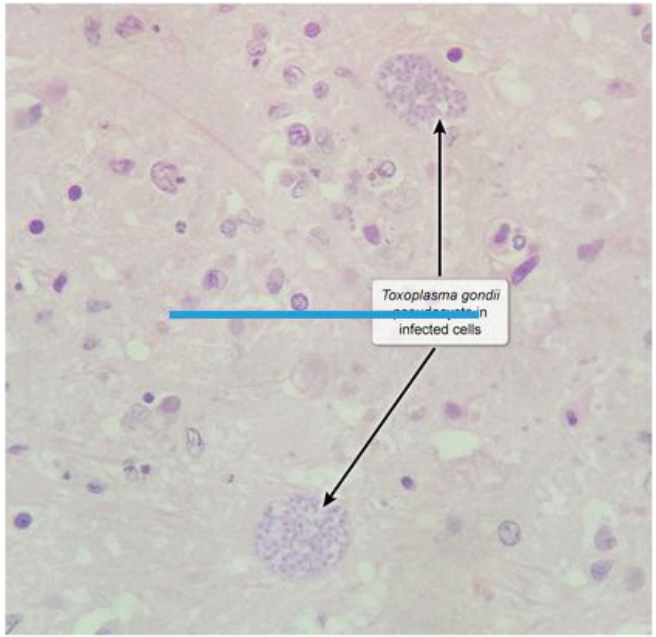
## Exhibit Display

**Cerebral toxoplasmosis**

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Cerebral arteriovenous malformations (AVMs) are vascular malformations histologically characterized by a



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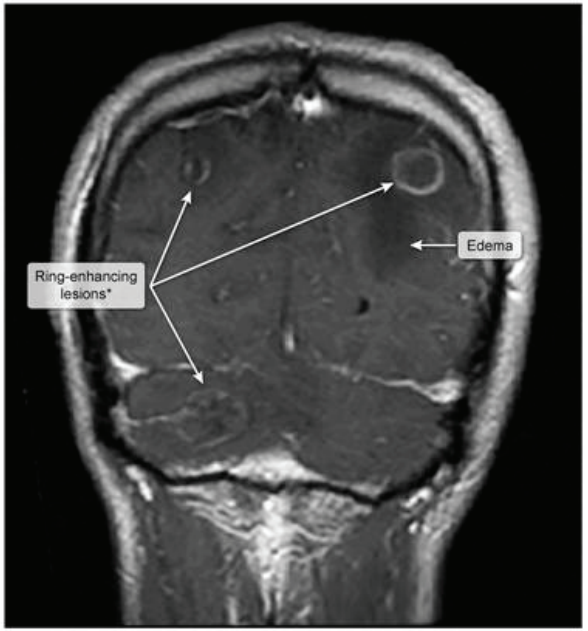
## Exhibit Display

**Cerebral toxoplasmosis**




*Necrosis with surrounding inflammation and *Toxoplasma* organisms ©UWorld

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Cerebral arteriovenous malformations (AVMs) are vascular malformations histologically characterized by a



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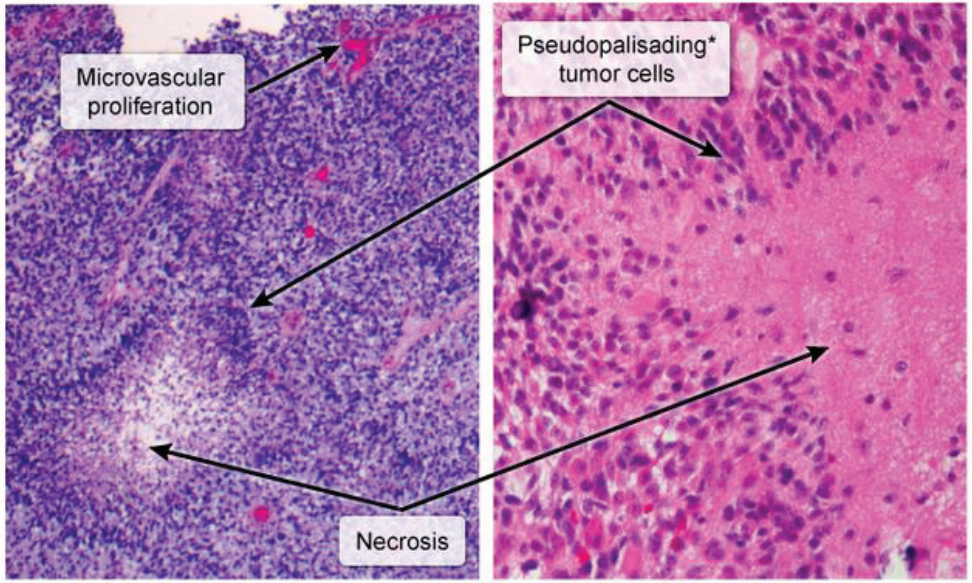
Exhibit Display

## Glioblastoma




*Tumor cells arranged around central necrosis.

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Cerebral arteriovenous malformations (AVMs) are vascular malformations histologically characterized by a



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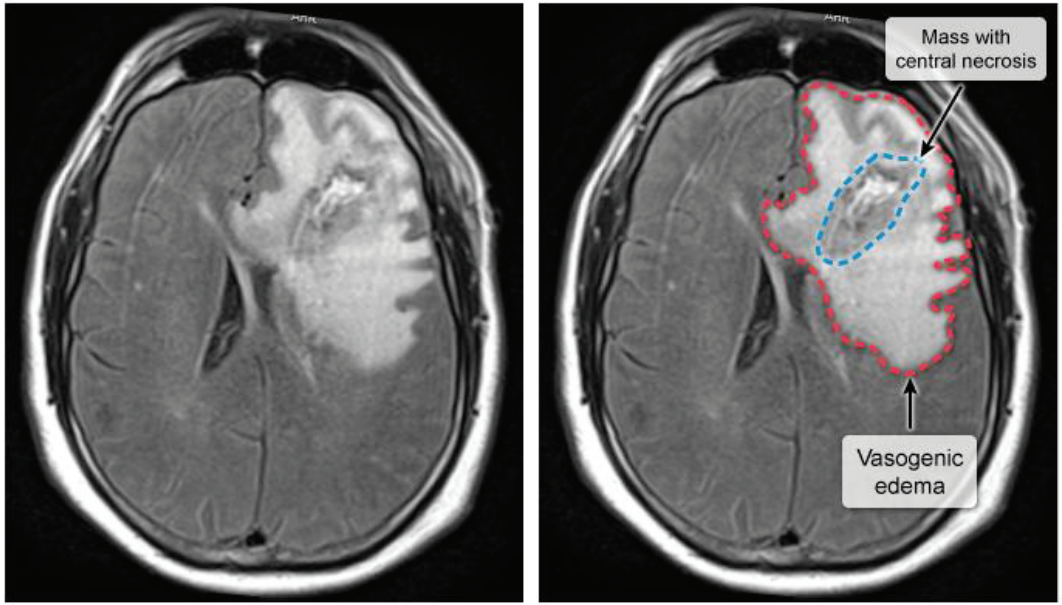
Exhibit Display

## Glioblastoma

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Cerebral arteriovenous malformations (AVMs) are vascular malformations histologically characterized by a



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**(Choice C)** Histologic findings in cerebral *Toxoplasma gondii* infection include necrotic debris with surrounding inflammation, tachyzoites, and pseudocysts of bradyzoites. Although seizures and headaches are a frequent manifestation, CNS toxoplasmosis usually occurs in immunocompromised patients. Imaging would likely reveal ring-enhancing lesions.

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**Educational objective:**
Cerebral arteriovenous malformations (AVMs) are vascular malformations histologically characterized by a tangle of abnormal vessels, including large veins with thickened walls and irregular arteries. AVMs may present with intracranial hemorrhage, headache, and/or seizures. Radiologic findings include abnormal vasculature with a "bag of worms" appearance and multiple dark flow voids.

| Anatomy | Nervous System | Av malformation |
|---|---|---|
| Subject | System | Topic |


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A 46-year-old man comes to the office with left upper limb weakness and numbness. He has had chronic neck pain since being involved in a motor vehicle collision 4 years ago. He has no other medical problems. Neurological evaluation reveals that the tendon reflex shown in the image below is absent. Reflexes in the right upper extremity and both lower extremities are normal.

Imaging studies reveal degenerative changes in the spine causing mild spinal cord compression. Which of the following spinal segments is most likely affected in this patient?

A. C3-C4
B. C5-C6
C. C7-C8


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Imaging studies reveal degenerative changes in the spine causing mild spinal cord compression. Which of the following spinal segments is most likely affected in this patient?

A. C3-C4
B. C5-C6
C. C7-C8
D. C8-T1
E. T1-T2

Submit



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Imaging studies reveal degenerative changes in the spine causing mild spinal cord compression. Which of the following spinal segments is most likely affected in this patient?

A. C3-C4 (4%)
B. C5-C6 (85%)
C. C7-C8 (6%)
D. C8-T1 (2%)
E. T1-T2 (0%)

Correct

85%

32 secs

11/07/2020



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| Myotomes & reflexes of the upper extremity | | |
|---|---|---|
| Myotomes | C4 | Shoulder/scapula elevation |
| | C5 | Shoulder abduction |
| | C5, C6 | Elbow flexion, wrist extension |
| | C7 | Elbow extension, finger extension |
| | C8 | Wrist flexion, finger flexion |
| | T1 | Finger abduction |
| Reflexes | C5, C6 | Biceps & brachioradialis reflexes |
| | C7, C8 | Triceps reflex |

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This patient has an absent **biceps reflex**. The test is performed by quickly tapping a reflex hammer against the biceps brachii tendon as it passes through the cubital fossa. This action activates the muscle's


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This patient has an absent **biceps reflex**. The test is performed by quickly tapping a reflex hammer against the biceps brachii tendon as it passes through the cubital fossa. This action activates the muscle's stretch receptors that communicate via the musculocutaneous nerve with lower motor neurons in the anterior horn of the **C5-C6 spinal level**.

Axons from these motor neurons return along the musculocutaneous nerve and cause involuntary biceps muscle contraction and jerking of the forearm. The C5-C6 nerves also control the brachioradialis reflex. A stronger than normal reflex suggests an upper motor neuron lesion whereas an absent or decreased reflex indicates a lower motor neuron lesion at the corresponding spinal cord level.

**(Choice A)** The C3-C4 cervical nerves provide innervation to the diaphragm but do not mediate any specific reflexes.

**(Choices C, D, and E)** The C7, C8, and T1 spinal nerve roots form the median and ulnar nerves, which provide motor innervation to the wrist and hand. The T1 and T2 thoracic nerves innervate the rib muscles around the sternum, parts of the axilla, and part of the scapula. However, none of these spinal nerves mediate significant reflexes.

**Educational objective:**



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**Educational objective:**
The C5-C6 spinal nerves mediate the biceps and brachioradialis reflexes.

| Anatomy | Nervous System | Radiculopathy |
|---|---|---|
| Subject | System | Topic |

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A 68-year-old man with a history of Parkinson disease is hospitalized for pneumonia and sepsis. The patient is treated with intravenous (IV) fluids and antibiotics. He is also started on an infusion of IV dopamine for hemodynamic support. Although the manifestations of Parkinson disease are attributed to dopaminergic neuron degeneration in the substantia nigra, IV dopamine does not improve this patient's Parkinson symptoms. Which of the following cell structures accounts for this lack of responsiveness?

- A. Desmosomes
- B. Fenestrae
- C. Gap junctions
- D. Hemidesmosomes
- E. Intermediate junctions
- F. Tight junctions

Submit



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A 68-year-old man with a history of Parkinson disease is hospitalized for pneumonia and sepsis. The patient is treated with intravenous (IV) fluids and antibiotics. He is also started on an infusion of IV dopamine for hemodynamic support. Although the manifestations of Parkinson disease are attributed to dopaminergic neuron degeneration in the substantia nigra, IV dopamine does not improve this patient's Parkinson symptoms. Which of the following cell structures accounts for this lack of responsiveness?

- A. Desmosomes (1%)
- B. Fenestrae (4%)
- C. Gap junctions (7%)
- D. Hemidesmosomes (1%)
- E. Intermediate junctions (0%)
- ✓ F. Tight junctions (85%)

Correct

85%
Answered correctly

45 secs
Time Spent

02/05/2021
Last Updated



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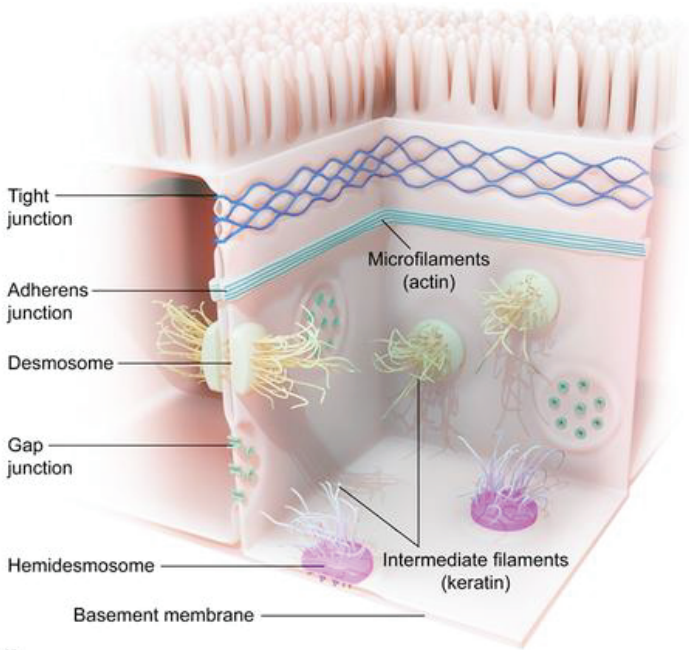
Exhibit Display

Cell junctions

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This patient's Parkinson symptoms do not improve with intravenous dopamine infusion because dopamine is unable to cross the blood-brain barrier. The **blood-brain barrier** is formed by tight junctions between nonfenestrated capillary endothelial cells that prevent the **paracellular** passage of fluid and solutes. **Tight junctions**, also known as zonulae occludentes, are composed of transmembrane proteins (eg, claudins and occludins) that associate with actin filaments, forming a **beltlike seal** around the apical intercellular space. This seal only permits the passage of substances from the blood to the brain via transcellular movement.

Transcellular movement of dopamine is limited by the molecule's low lipid solubility and the lack of dopamine-specific transport carriers in capillary endothelial cells of the blood-brain barrier. L-DOPA (dopamine precursor) also has low lipid solubility, but it is able to enter the brain due to its high affinity for the large neutral amino acid transporter.

**(Choice A)** Desmosomes (maculae adherentes) are spotlike junctions that anchor adjacent cells together via keratin intermediate filament interactions. Autoantibodies against desmosomes in the stratum spinosum of the skin cause pemphigus vulgaris.

**(Choice B)** Fenestrae are small pores within endothelial cells that allow free fluid exchange between the intravascular and extravascular spaces. They are found in capillaries perfusing the intestine, renal tubules,


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**(Choice B)** Fenestrae are small pores within endothelial cells that allow free fluid exchange between the intravascular and extravascular spaces. They are found in capillaries perfusing the intestine, renal tubules, and endocrine glands.

**(Choice C)** Gap junctions are composed of connexin proteins that create channels between cells, permitting the free passage of small ions (eg, $Ca^{2+}$) and molecules.

**(Choice D)** Hemidesmosomes are similar to desmosomes but bind the basal layer of epithelial cells to the basement membrane. Autoantibodies against hemidesmosomes in the skin cause bullous pemphigoid.

**(Choice E)** Intermediate junctions (zonula adherens or belt desmosomes) are located below tight junctions and form a beltlike anchor between adjacent cells in association with actin microfilaments.

**Educational objective:**
The blood-brain barrier is formed by tight junctions between nonfenestrated capillary endothelial cells that prevent the paracellular passage of fluid and solutes. This barrier only permits the passage of substances from the blood to the brain via transcellular movement across the endothelial plasma membrane, which is limited by diffusion or carrier-mediated transport.

**References**


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A 36-year-old woman comes to the office due to firm, nontender swelling of her right cheek for the past 4 months. The patient has had no fever, runny nose, sore throat, or cough. She drinks a glass of wine with dinner on most nights but does not use tobacco. Physical examination shows fullness of the preauricular space on the right side. An MRI of the region identifies a 2.2-cm mass in the right parotid gland, and a follow-up core needle biopsy shows the lesion to be neoplastic. If left untreated, this patient is most likely to develop which of the following?

A. Bitemporal hemianopsia
B. Facial droop
C. Facial numbness
D. Hoarseness
E. Horner syndrome
F. Strabismus

Submit



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www.ncbi.nlm.nih.gov/pubmed/22686334

A 36-year-old woman comes to the office due to firm, nontender swelling of her right cheek for the past 4 months. The patient has had no fever, runny nose, sore throat, or cough. She drinks a glass of wine with dinner on most nights but does not use tobacco. Physical examination shows fullness of the preauricular space on the right side. An MRI of the region identifies a 2.2-cm mass in the right parotid gland, and a follow-up core needle biopsy shows the lesion to be neoplastic. If left untreated, this patient is most likely to develop which of the following?

A. ~~Bitemporal hemianopsia~~ (0%)
✓ B. Facial droop (69%)
C. Facial numbness (19%)
D. Hoarseness (4%)
E. Horner syndrome (4%)
F. Strabismus (0%)


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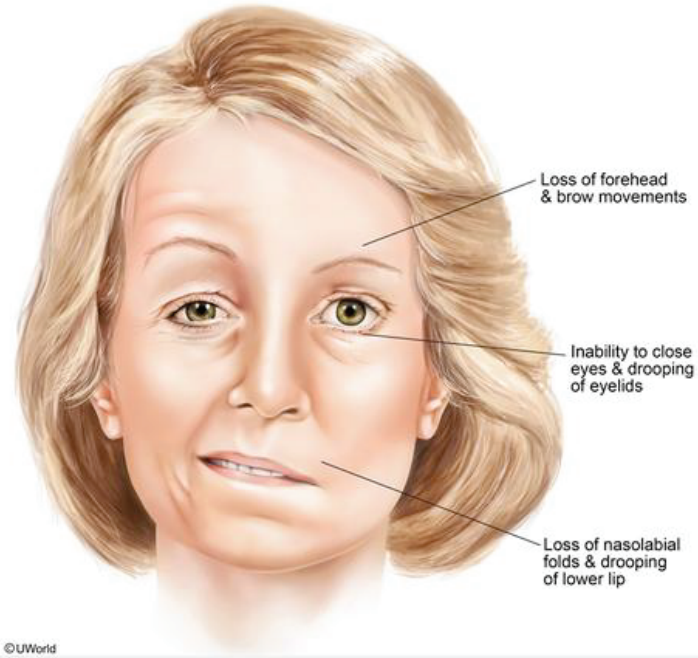
## Exhibit Display

**Peripheral facial palsy**

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The **extracranial** portion of the **facial nerve (CN VII)** carries motor innervation to the muscles of facial expression. This nerve exits the skull through the **stylomastoid foramen** and courses within the substance of the parotid gland. Within this gland, the facial nerve divides into its 5 terminal branches (temporal, zygomatic, buccal, mandibular, and cervical). Parotid gland tumors can compress and disrupt the ipsilateral facial nerve and its branches, causing **facial droop**. In fact, most parotid gland tumors causing facial nerve paralysis are **malignant** neoplasms.

**(Choice A)** Bitemporal hemianopsia typically results from tumors (eg, craniopharyngioma, pituitary adenoma) within the sella turcica that compress the optic chiasm.

**(Choice C)** The trigeminal nerve (via its 3 branches) provides sensation to the face and motor innervation to the muscles of mastication. This nerve follows a deep course and is unlikely to be damaged by a tumor of the parotid gland.

**(Choice D)** The recurrent laryngeal nerve is a branch of the vagus nerve that loops below the aortic arch on the left and below the subclavian artery on the right to provide motor innervation to the laryngeal muscles. During **thyroid surgery**, this nerve may be damaged due to its proximity to the inferior thyroid artery. Unilateral nerve injury often causes hoarseness, whereas bilateral injury may cause inspiratory



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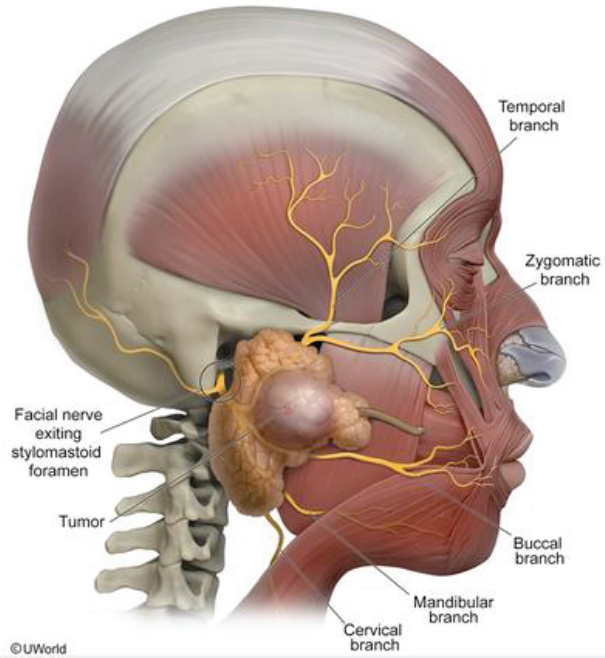
Exhibit Display

Parotid tumor compressing facial nerve

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muscles. During **thyroid surgery**, this nerve may be damaged due to its proximity to the inferior thyroid artery. Unilateral nerve injury often causes hoarseness, whereas bilateral injury may cause inspiratory stridor and respiratory distress due to complete **vocal cord paralysis**.

**(Choice E)** Horner syndrome presents with partial ptosis, miosis, and anhidrosis due to interruption of the sympathetic innervation to the head. This can occur with lesions affecting the lateral hypothalamus, hypothalamospinal tract, paravertebral sympathetic chain/stellate ganglion (eg, Pancoast tumor), or internal carotid artery (eg, carotid dissection).

**(Choice F)** Strabismus (improper alignment of the eyes) can result from disorders of the extraocular muscles or the nerves that innervate them (CN III, IV, or VI).

**Educational objective:**

The facial nerve (CN VII) exits the stylomastoid foramen and courses through the substance of the parotid gland, where it divides into its 5 terminal branches that innervate the muscles of facial expression. Malignant tumors of the parotid gland often compress and disrupt the facial nerve and its branches, causing ipsilateral facial droop.

**References**

- The presence of facial nerve weakness on diagnosis of a parotid gland malignant process



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A 22-year-old man comes to the emergency department due to sudden-onset pain and stiffness on one side of his neck. He was diagnosed with a psychiatric disorder 2 days ago and has been adherent with his newly prescribed medication. For the past few months, the patient has heard voices telling him to quit his job, and he believes that his girlfriend's parents are monitoring his sexual thoughts with a special device. He has been socially withdrawn and has difficulty showering regularly. Vital signs are within normal limits. The head is tilted to one side and cannot be straightened without considerable pain. The most likely cause of this patient's symptoms is antagonism of which of the following receptors?

A. Alpha-1 adrenergic
B. Dopaminergic D2
C. GABA-A
D. Histaminergic H1
E. Muscarinic M1
F. Serotonergic 5-HT2A


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side of his neck. He was diagnosed with a psychiatric disorder 2 days ago and has been adherent with his newly prescribed medication. For the past few months, the patient has heard voices telling him to quit his job, and he believes that his girlfriend's parents are monitoring his sexual thoughts with a special device. He has been socially withdrawn and has difficulty showering regularly. Vital signs are within normal limits. The head is tilted to one side and cannot be straightened without considerable pain. The most likely cause of this patient's symptoms is antagonism of which of the following receptors?

A. Alpha-1 adrenergic (0%)
B. Dopaminergic D2 (75%)
C. GABA-A (8%)
D. Histaminergic H1 (0%)
E. Muscarinic M1 (6%)
F. Serotonergic 5-HT2A (7%)

Correct

75%
49 secs
12/03/2020



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This patient is experiencing an **acute dystonic reaction** (ie, spasmodic torticollis), a type of extrapyramidal symptom (EPS) most likely due to recent initiation of **antipsychotic medication**. Acute dystonia can develop abruptly anytime between 4 hours and 4 days after receiving an antipsychotic medication. The condition is characterized by a sudden, involuntary contraction of a major muscle group. Other examples of acute dystonia include oculogyric crisis (forced, sustained elevation of the eyes in an upward position), opisthotonus (arching of the back with the head thrown backward), and, rarely, laryngospasm. The risk is highest with high-potency, first-generation antipsychotics (eg, haloperidol, fluphenazine).

Acute dystonic reactions are theorized to result from the antipsychotic property of **D2 antagonism** in the **nigrostriatal pathway**. In the striatum, the inhibitory effects of dopaminergic neurons (D2) are normally balanced by the excitatory actions of muscarinic cholinergic neurons (M1). Strong dopaminergic blockade causes an excess of cholinergic activity, resulting in extrapyramidal side effects (eg, acute dystonic reactions, akathisia, parkinsonism). Medications with M1 receptor antagonist properties, such as benztropine or the antihistamine diphenhydramine, help re-establish the dopaminergic-cholinergic balance and effectively treat acute dystonia.

**(Choice A)** Blockade of alpha-1 adrenergic receptors causes orthostatic hypotension and dizziness.

**(Choice C)** Flumazenil, a benzodiazepine GABA-A receptor antagonist, can be used to treat



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**(Choice A)** Blockade of alpha-1 adrenergic receptors causes orthostatic hypotension and dizziness.

**(Choice C)** Flumazenil, a benzodiazepine GABA-A receptor antagonist, can be used to treat benzodiazepine overdose. However, it may precipitate withdrawal seizures in patients with chronic benzodiazepine use.

**(Choice D)** Antagonism of central histamine H1 receptors causes sedation and weight gain.

**(Choice E)** Antagonism of muscarinic receptors causes anticholinergic side effects (eg, confusion, dry mouth, urinary retention). Low-potency antipsychotics (eg, chlorpromazine, thioridazine) are more likely to cause these effects due to their strong blockade of central and peripheral muscarinic cholinergic receptors.

**(Choice F)** Second-generation antipsychotics antagonize serotonergic 5-HT2A, but this does not typically cause dystonia.

**Educational objective:**
Acute extrapyramidal symptoms (eg, dystonia, akathisia, parkinsonism) are due to D2 blockade in the nigrostriatal pathway. First-generation, high-potency antipsychotics (eg, haloperidol, fluphenazine) strongly block D2 receptors and are most likely to cause extrapyramidal symptoms.

**References**


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A 56-year-old woman is brought to the emergency department with sudden onset of headache and partial loss of vision. She has a 3-year history of atrial fibrillation. Physical examination shows a visual field defect involving the black areas illustrated below.

This patient most likely has occlusion of which of the following arteries?

A. Anterior cerebral
B. Central retinal
C. Middle cerebral
D. Posterior cerebral
E. Posterior inferior cerebellar


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loss of vision. She has a 3-year history of atrial fibrillation. Physical examination shows a visual field defect involving the black areas illustrated below.

This patient most likely has occlusion of which of the following arteries?

A. Anterior cerebral (3%)
B. Central retinal (1%)
C. Middle cerebral (11%)
D. Posterior cerebral (78%)
E. Posterior inferior cerebellar (4%)

Correct
78%
38 secs
01/11/2021


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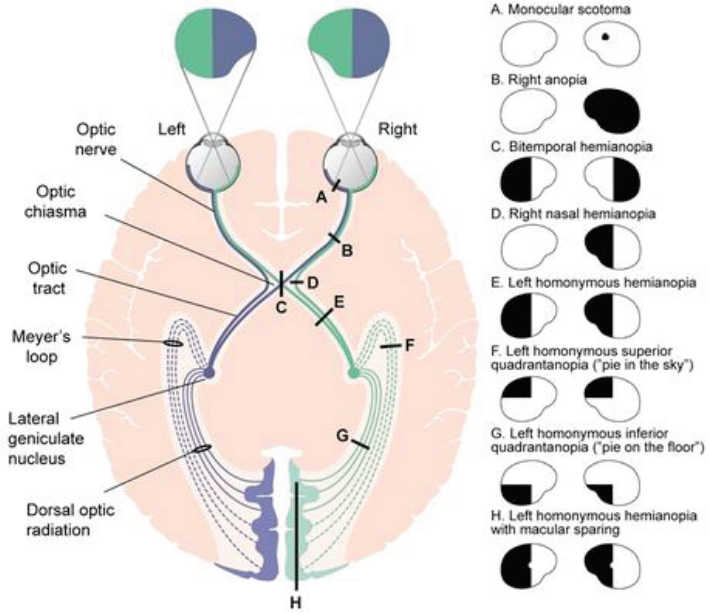
Exhibit Display

Visual pathways from above

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The described vision defect is consistent with an occlusion of the posterior cerebral artery (PCA), most likely from an embolic event given this patient's history of atrial fibrillation. The PCA supplies the occipital lobe, which contains the striate or primary visual cortex. The striate cortex of each hemisphere receives information about the contralateral visual field from the ipsilateral lateral geniculate nucleus via the optic radiation. Specifically, the cuneus gyrus of the striate cortex receives information from the upper retina (lower visual field), while the lingual gyrus of the striate cortex receives information from the lower retina (upper visual field).

Occlusion of the PCA leads to ischemic injury to the ipsilateral striate cortex, producing a contralateral homonymous hemianopia with macular sparing. The macula is spared because collateral blood is supplied by the middle cerebral artery to the occipital pole, which processes central visual information. Unilateral infarcts involving only the cuneus gyrus or the lingual gyrus will produce a lower or upper quadrantanopia, respectively.

**(Choice A)** Anterior cerebral artery occlusion manifests as contralateral weakness that predominantly affects the lower extremity.

**(Choice B)** Occlusion of the central retinal artery leads to sudden, painless, and complete loss of vision in the affected eye.


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affects the lower extremity.

**(Choice B)** Occlusion of the central retinal artery leads to sudden, painless, and complete loss of vision in the affected eye.

**(Choice C)** Middle cerebral artery stroke is characterized by contralateral motor and sensory deficits (more pronounced in the upper than lower limb) and homonymous hemianopia **with macular involvement**.

**(Choice E)** Occlusion of the posterior inferior cerebellar artery leads to lateral medullary (Wallenberg) syndrome. It is characterized by contralateral loss of pain and temperature sensation; ipsilateral deficits of CN V, VIII, IX, X, and XI; and Horner's syndrome.

**Educational objective:**
Lesions of the occipital cortex (eg, posterior cerebral artery occlusion) can produce contralateral homonymous hemianopia with macular sparing.

| Anatomy | Nervous System | Visual pathway |
|---|---|---|
| Subject | System | Topic |

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A 6-year-old boy is brought to the emergency department by his parents with a 2-day history of fever and headaches. The parents report that he vomited once this afternoon. All of his vaccinations are up-to-date and he has no significant past medical history. His temperature is 38.7 C (102 F). Examination shows mild pharyngeal erythema in addition to neck stiffness. Cerebrospinal fluid analysis reveals the following:

| | |
|---|---|
| Glucose | 65 mg/dL |
| Protein | 85 mg/dL |
| Leukocytes | 300/mm$^3$ |
| Differential | |
| Neutrophils | 15% |
| Lymphocytes | 85% |
| Red blood cells | none |


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| | |
|---|---|
| Neutrophils | 15% |
| Lymphocytes | 85% |
| Red blood cells | none |

Which of the following infectious agents is most likely to have caused this patient's illness?

A. Coronavirus
B. *Cryptococcus neoformans*
C. Enterovirus
D. Mumps virus
E. *Neisseria meningitidis*
F. *Streptococcus agalactiae*
G. *Streptococcus pneumoniae*

Submit



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| | |
|---|---|
| Lymphocytes | 85% |
| Red blood cells | none |

Which of the following infectious agents is most likely to have caused this patient's illness?

- A. Coronavirus (13%)
- B. ~~*Cryptococcus neoformans*~~ (4%)
- ✓ C. Enterovirus (56%)
- D. Mumps virus (7%)
- E. ~~*Neisseria meningitidis*~~ (6%)
- F. ~~*Streptococcus agalactiae*~~ (1%)
- G. ~~*Streptococcus pneumoniae*~~ (8%)

Correct

56%

01 min, 21 secs

09/28/2020



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| Differences between bacterial & viral meningitis | | |
|---|---|---|
| | **Viral** | **Bacterial** |
| **Common microbes** | • **Enteroviruses** (most common)<br>• Arboviruses<br>• Herpes simplex virus type 2 | • **Adults**: *Streptococcus pneumoniae* & *Neisseria meningitidis*<br>• **Neonates**: Group B *Streptococcus* & gram-negative bacilli |
| **CSF cell differential** | • WBC count often **<500** cells/mm$^3$<br>• Lymphocytic predominance | • WBC count often **>1000** cells/mm$^3$<br>• Neutrophilic predominance |
| **CSF glucose & protein** | • Glucose levels are **normal** or slightly reduced<br>• Protein generally <150 mg/dL | • Glucose levels **<45 mg/dL**<br>• Protein is often >250 mg/dL |
| **CSF Gram** | | |



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| | | |
|---|---|---|
| protein | • Protein generally <150 mg/dL | |
| **CSF Gram stain & culture** | • No organisms identified | • Often positive for a specific organism |

**CSF** = cerebrospinal fluid; **WBC** = white blood cell.

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This child has clinical evidence of meningitis (fever, headache, vomiting, stiff neck). Analysis of the cerebrospinal fluid (CSF) shows **normal** glucose, marginally elevated protein, and pleocytosis with a **lymphocytic** predominance. This pattern suggests **aseptic meningitis**, which is usually viral in etiology. **Enteroviruses** (eg, coxsackievirus, echovirus, poliovirus) are responsible for >90% of cases. Clinical symptoms are similar to meningitis caused by bacterial or fungal pathogens. However, aseptic meningitis is generally **less severe**, and focal neurologic signs, seizures, and alterations in mental status are absent. The presence of any of these should prompt consideration of other conditions, including bacterial meningitis, encephalitis, and intracranial hemorrhage. A negative Gram stain and **sterile culture** will further support the diagnosis of aseptic meningitis.

**(Choice A)** Coronavirus is a common cause of cold symptoms. It is not a common cause of viral meningitis.



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meningitis.

**(Choice B)** *Cryptococcus neoformans* is a common cause of meningitis in immunocompromised patients (eg, AIDS patients). The diagnosis is made by testing for cryptococcal antigens or by identifying India ink-stained organisms in the CSF.

**(Choice D)** The mumps virus can cause aseptic meningitis, but this would be extremely unlikely in this fully immunized child. Meningitis caused by mumps is accompanied by parotitis in 50% of cases.

**(Choices E, F, and G)** *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most common causes of bacterial meningitis in adults; *S agalactiae* (group B *Streptococcus*) is the most common cause of meningitis in neonates. Bacterial and viral meningitis both cause fever, nuchal rigidity, and headache. However, this patient's CSF analysis is more suggestive of aseptic meningitis.

**Educational objective:**

Fever; meningeal signs (eg, headache, neck stiffness); and cerebrospinal fluid that shows lymphocytic pleocytosis, a modestly elevated protein level, and normal glucose are suggestive of aseptic meningitis. Enteroviruses are the most common cause of aseptic meningitis.

**References**

- Viral meningitis.



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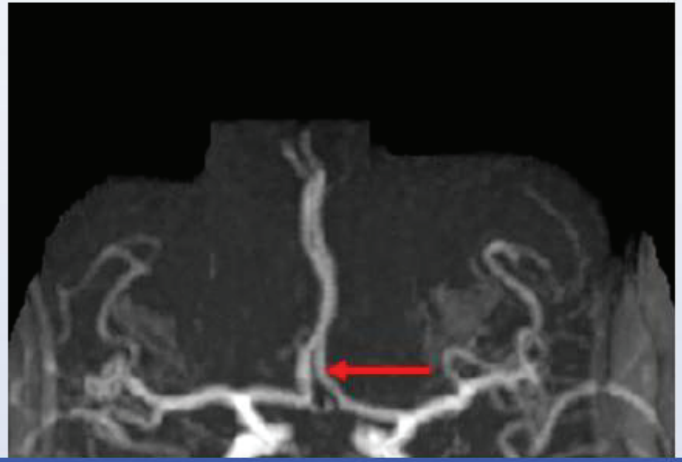
A 68-year-old man is evaluated for visual loss in the left eye that resolved spontaneously within several hours. The patient has a history of hypertension, type 2 diabetes mellitus, coronary artery disease, and ischemic cardiomyopathy. He has smoked a pack of cigarettes daily for the past 40 years. Physical examination reveals a left carotid bruit but no neurologic deficits. A carotid duplex ultrasound shows 85% stenosis of the left internal carotid artery, and carotid angiography with stenting is performed. During the procedure, atherosclerotic debris embolize to the artery shown (red arrow) on the cerebral magnetic resonance angiograph below.





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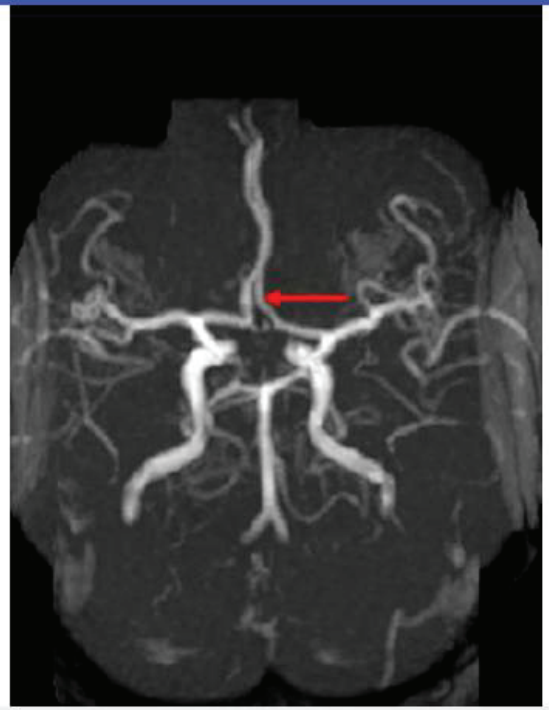

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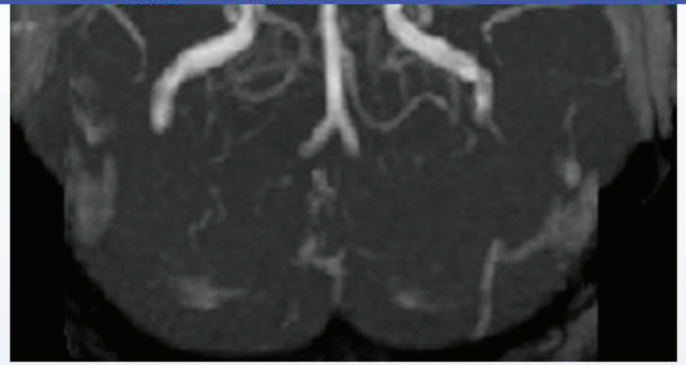

Which of the following actions is most likely to be impaired in this patient?

A. Climbing stairs
B. Gripping
C. Speaking
D. Swallowing food
E. Whistling



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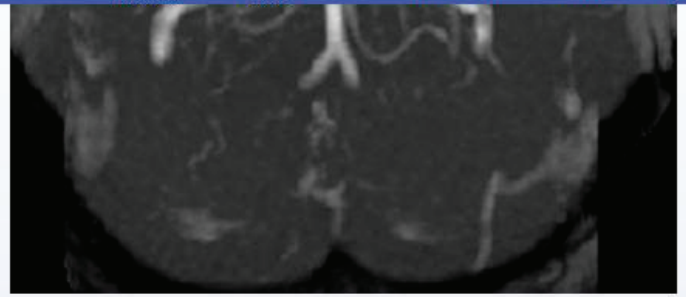

Which of the following actions is most likely to be impaired in this patient?

- A. Climbing stairs (76%)
- B. Gripping (5%)
- C. Speaking (11%)
- D. Swallowing food (3%)
- E. Whistling (3%)

Correct

76%

23 secs

11/24/2020



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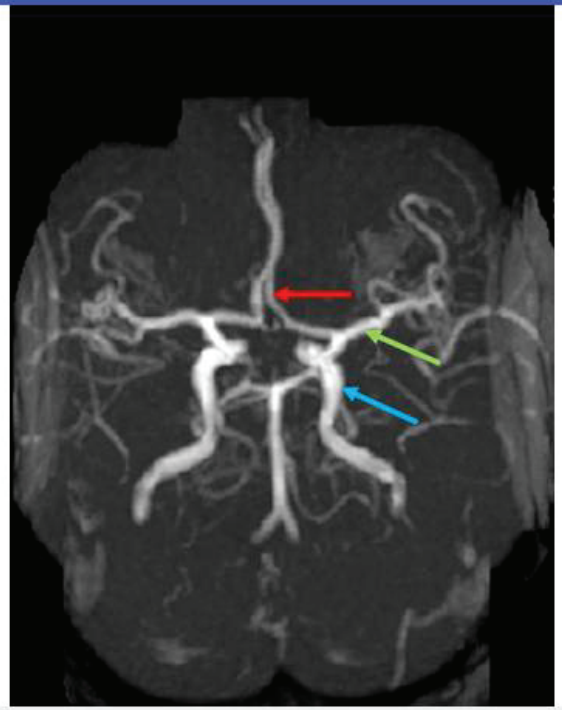

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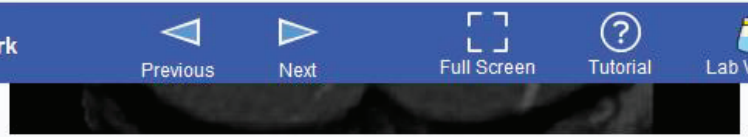

This cerebral magnetic resonance angiogram shows a 3D reconstruction of the circle of Willis, with the top representing superior regions and the bottom representing inferior regions. The internal carotid arteries are the large vessels seen bilaterally near the center of the image (blue arrow). Each gives off a middle cerebral artery (green arrow) to supply lateral brain regions and an **anterior cerebral artery** (red arrow), which extends medially and then superiorly. Each anterior cerebral artery supplies the medial region of the ipsilateral hemisphere, from the frontal pole to the parietooccipital sulcus.

Occlusion of the anterior cerebral artery would affect sensory and motor function of the **contralateral leg and foot** while predominantly sparing the contralateral arm/face (cortical homunculus). Patients with bilateral anterior cerebral artery occlusion can also develop significant **behavioral symptoms** (eg, abulia) and **urinary incontinence** if the frontal micturition center (eg, medial frontal lobe/cingulate gyrus) is affected.

**(Choices B, C, D, and E)** Occlusion of the middle cerebral artery would affect motor control of the hand (eg, gripping), face/mouth (eg, whistling), and throat (eg, swallowing) out of proportion to the leg. It can also result in Broca aphasia (due to damage of the dominant frontal lobe), anosognosia and spatial neglect of the contralateral side (due to damage of the nondominant parietal lobe), conjugate gaze deviation toward



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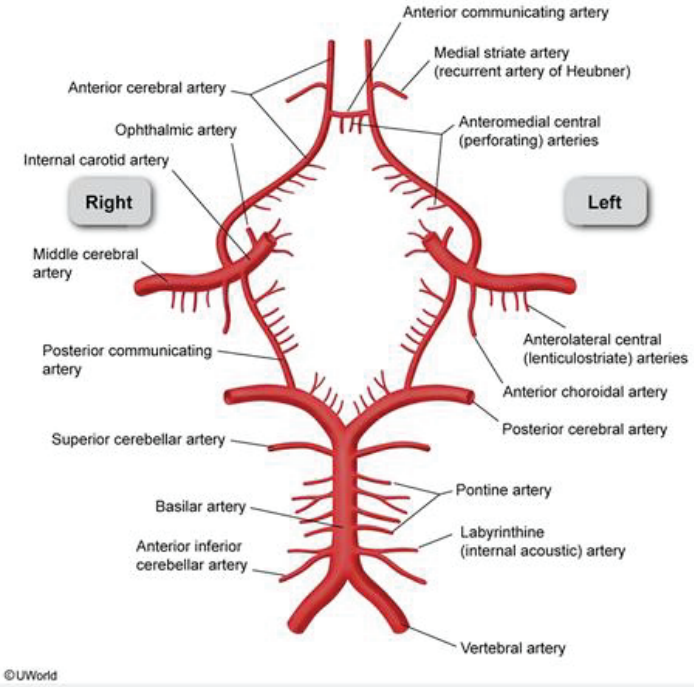


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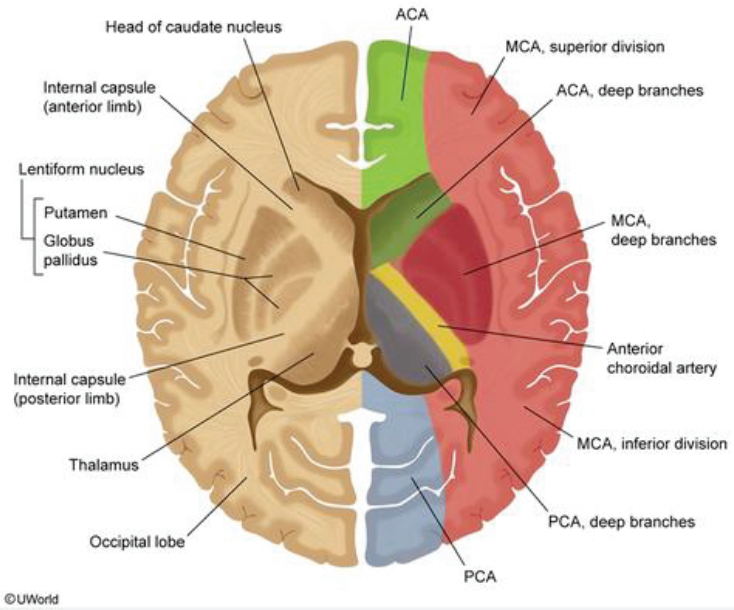
## Exhibit Display

Blood supply to the cerebral hemispheres  Cerebral hemisphere blood supply

### Blood supply to the cerebral hemispheres

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## Exhibit Display

Blood supply to the cerebral hemispheres Cerebral hemisphere blood supply

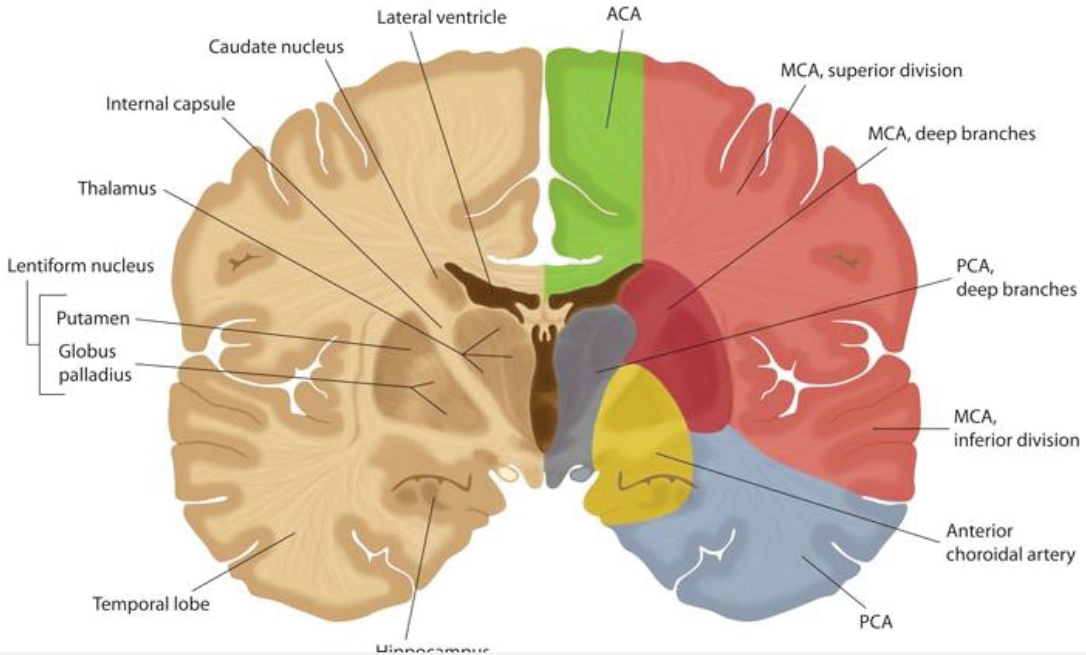


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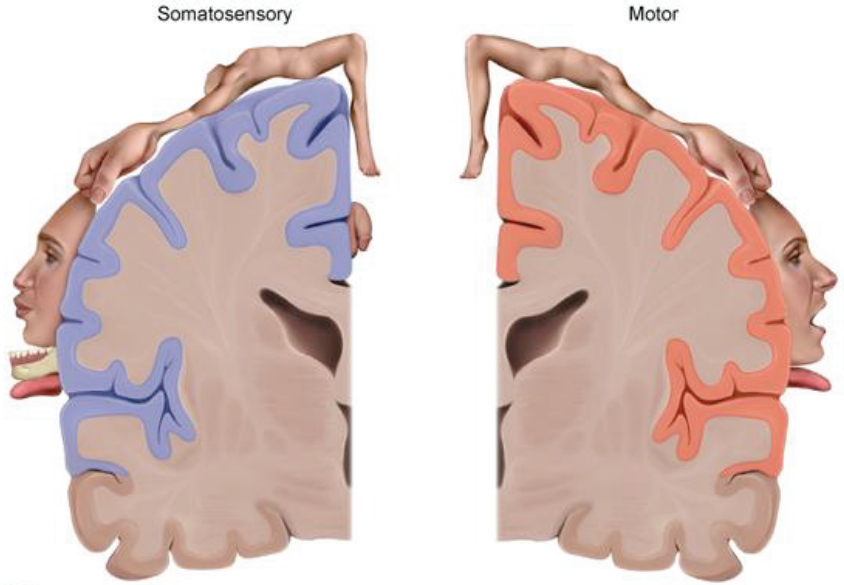
Exhibit Display

## Homunculus

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and **urinary incontinence** if the frontal micturition center (eg, medial frontal lobe/cingulate gyrus) is affected.

**(Choices B, C, D, and E)** Occlusion of the middle cerebral artery would affect motor control of the hand (eg, gripping), face/mouth (eg, whistling), and throat (eg, swallowing) out of proportion to the leg. It can also result in Broca aphasia (due to damage of the dominant frontal lobe), anosognosia and spatial neglect of the contralateral side (due to damage of the nondominant parietal lobe), conjugate gaze deviation toward the side of the stroke, and contralateral homonymous hemianopsia (due to damage of the optic radiations in the subcortical temporoparietal lobe).

**Educational objective:**

The anterior cerebral arteries supply the medial portions of the 2 hemispheres (frontal and parietal lobes). Occlusion can cause contralateral motor and sensory deficits of the lower extremities, behavioral changes, and urinary incontinence.

**References**

- Anterior cerebral artery and Heubner's artery territory infarction.

Anatomy Nervous System Ischemic stroke



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A 32-year-old man is brought to the emergency department due to fever, agitation, and disorientation. According to his family, the patient has been acting strangely and seeing and hearing things that do not exist. He also drools excessively and has severe, painful throat spasms when he attempts to eat or drink. The patient returned 4 weeks ago from a camping trip in New Mexico. Physical examination shows a confused and combative patient with mydriasis and neck rigidity. Which of the following acts as an entry receptor for the causative agent of this patient's condition?

A. B-lymphocyte CD21
B. Muscle acetylcholine receptors
C. Nasopharyngeal intracellular adhesion molecule-1
D. Respiratory epithelial sialic acids
E. Vascular endothelial integrins

Submit



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A 32-year-old man is brought to the emergency department due to fever, agitation, and disorientation. According to his family, the patient has been acting strangely and seeing and hearing things that do not exist. He also drools excessively and has severe, painful throat spasms when he attempts to eat or drink. The patient returned 4 weeks ago from a camping trip in New Mexico. Physical examination shows a confused and combative patient with mydriasis and neck rigidity. Which of the following acts as an entry receptor for the causative agent of this patient's condition?

- A. ~~B-lymphocyte CD21~~ (3%)
- ✓ B. Muscle acetylcholine receptors (61%)
- C. ~~Nasopharyngeal intracellular adhesion molecule-1~~ (16%)
- D. Respiratory epithelial sialic acids (9%)
- ✗ E. Vascular endothelial integrins (10%)

Incorrect
Correct answer
B

61%
Answered correctly

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Time Spent

09/12/2020
Last Updated



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| Virion | Cellular receptor |
|---|---|
| Cytomegalovirus | Cellular integrins |
| Epstein-Barr virus | CR2 (CD21) |
| HIV | CD4 and CXCR4/CCR5 |
| Rabies virus | Nicotinic acetylcholine receptor |
| Rhinovirus | ICAM1 (CD54) |

**ICAM1** = intracellular adhesion molecule-1.

This patient's progressive agitation, disorientation, and pharyngospasm raises strong suspicion for **rabies**, a fatal infection caused by a neurotrophic virus from the **Rhabdoviridae** family. Exposure usually occurs when patients come into contact with **contaminated saliva** from an infected animal (eg, dog, bat), which likely occurred during this patient's camping trip in New Mexico. The virus contains a bullet-shaped envelope with knob-like glycoproteins that allow it to attach to the **nicotinic acetylcholine receptor** at the neuromuscular junction. The virus replicates locally within the muscle tissue of the bite wound for several days or weeks and then travels in a retrograde fashion through peripheral nerve axons to the dorsal root


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ganglia. From there, it rapidly ascends the spinal cord and infects the diencephalon, hippocampus, and brain stem.

Patients initially develop a nonspecific flu-like prodrome (fever, malaise, myalgias); paresthesias radiating proximally from a known wound site can be an important clue. When the virus enters the CNS, the infection typically evolves into rabies encephalitis, which is characterized by painful **pharyngeal spasms** leading to avoidance of water (**hydrophobia**), mental status changes, muscular rigidity, and autonomic dysfunction (pupil dilation, **hypersalivation**). Once symptoms of rabies encephalitis appear, postexposure prophylaxis is no longer effective and nearly all patients die.

**(Choice A)** Epstein-Barr virus binds to CD21 on inactive B-lymphocytes and results in infectious mononucleosis, which is usually characterized by sore throat, swollen lymph nodes, malaise, and atypical lymphocytosis. Because this virus is a member of the Herpesviridae family, initial infection is followed by a long-standing (usually asymptomatic) latent infection.

**(Choice C)** Rhinovirus binds intracellular adhesion molecule-1, which is found on nasopharyngeal and adenoid epithelial cells. It is associated with the common cold, not agitation, pharyngeal spasm, and hallucinations.


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**(Choice D)** The influenza virus has hemagglutinin glycoproteins that allow it to attach to sialic acids on the surface of the respiratory epithelium. Influenza is usually characterized by fever, myalgias, cough, headache, and respiratory symptoms; agitation and pharyngeal spasm are not typical features.

**(Choice E)** Cytomegalovirus binds to vascular endothelial integrins, leading to replication within endothelial cells. Initial cytomegalovirus infections are often asymptomatic, but patients can develop a mononucleosis-type syndrome (eg, lethargy, fever, atypical lymphocytosis). Psychosis and disorientation would be atypical.

**Educational objective:**

Rabies virus has a bullet-shaped envelope with knob-like glycoproteins that bind to nicotinic acetylcholine receptors. Once transmission occurs (usually due to a bite wound from an infected animal), the virus replicates locally in muscle tissue for several days or weeks before spreading in a retrograde fashion through the peripheral nerve axons to the central nervous system.

**References**


- The acetylcholine receptor as a cellular receptor for rabies virus.
- Rabies virus binding to the nicotinic acetylcholine receptor alpha subunit demonstrated by virus overlay protein binding assay.




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A 25-year-old man fractures his right tibia in a motor vehicle accident. His right leg is fixed in a cast and he requires underarm crutches to ambulate. Two weeks later, he comes to the clinic with right upper-extremity weakness and numbness. He has no neck or arm pain. The patient is concerned because he is right handed and cannot perform his duties as an electrician. On neurologic examination, there is diminished strength on extension of the right wrist with an absent triceps reflex. Injury to which of the following nerves is most likely responsible for this patient's symptoms?

- A. Accessory
- B. Axillary
- C. Long thoracic
- D. Median
- E. Radial
- F. Suprascapular

Submit



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A 25-year-old man fractures his right tibia in a motor vehicle accident. His right leg is fixed in a cast and he requires underarm crutches to ambulate. Two weeks later, he comes to the clinic with right upper-extremity weakness and numbness. He has no neck or arm pain. The patient is concerned because he is right handed and cannot perform his duties as an electrician. On neurologic examination, there is diminished strength on extension of the right wrist with an absent triceps reflex. Injury to which of the following nerves is most likely responsible for this patient's symptoms?

- A. Accessory (0%)
- ✗ B. Axillary (12%)
- C. Long thoracic (0%)
- D. Median (3%)
- ✓ E. Radial (81%)
- F. Suprascapular (0%)


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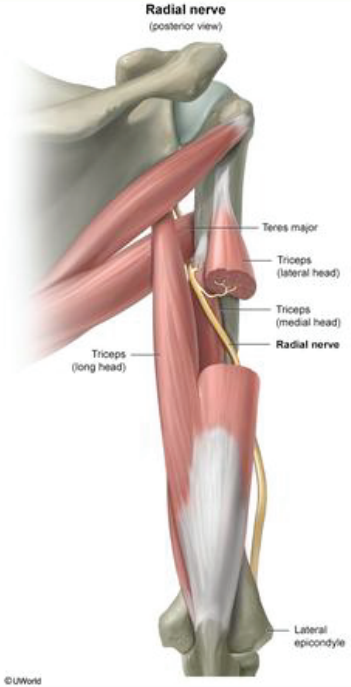


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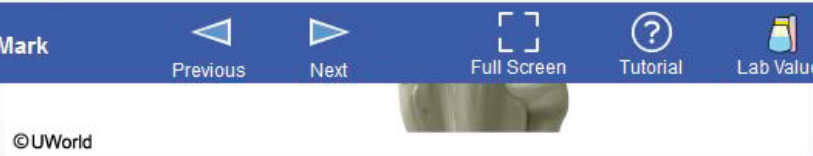


The radial nerve is derived from the C5-T1 spinal nerves and is one of the two final branches of the posterior cord of the brachial plexus. The nerve initially courses medial to the surgical neck of the humerus inferior to the teres major muscle within the axilla before entering the posterior arm to course between the long head of the triceps brachii and the posterior humerus.

**Proximal radial nerve injury** can occur at the nerve's superficial location within the axilla by repetitive pressure/trauma caused by an ill-fitting crutch (**"crutch palsy"**) or if an individual sleeps with the arm over a chair ("Saturday night palsy"). Injury to the nerve at this location may cause weakness or paralysis of the forearm, hand, and finger **extensor muscles** (eg, wrist drop, absent triceps reflex). Sensory loss may also be observed over the radial nerve distribution. Injuries to the proximal radial nerve as it crosses the posterior humerus (eg, midshaft humeral fractures) spare the triceps brachii, as the fibers innervating this muscle leave the nerve before it enters the radial groove.

**(Choice A)** The spinal accessory nerve (CN XI) exits the skull through the jugular foramen and courses over the levator scapulae muscle to innervate the sternocleidomastoid and trapezius muscles.

**(Choice B)** Fracture of the surgical neck of the humerus and anterior dislocation of the glenohumeral joint can cause injury to the axillary nerve. The resultant paralysis of the deltoid and teres minor muscles


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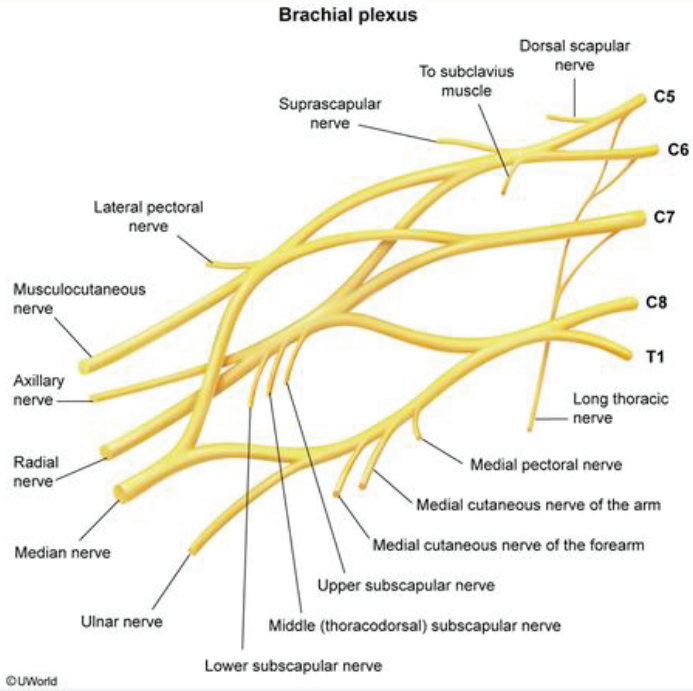


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can cause injury to the axillary nerve. The resultant paralysis of the deltoid and teres minor muscles



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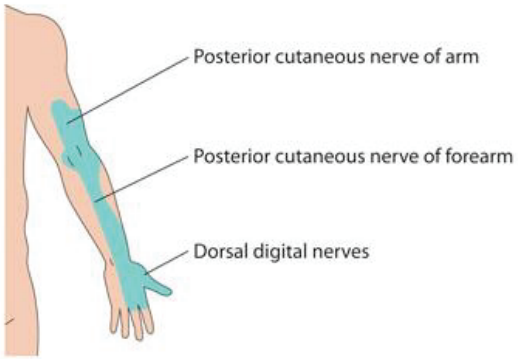
## Important nerves in the arm

| Nerve | Motor function | Region of sensory loss with neuropathy |
|---|---|---|
| Radial nerve | Extension at all arm, wrist, & finger joints below the shoulder, forearm supination, thumb abduction in plane of palm | |

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can cause injury to the axillary nerve. The resultant paralysis of the deltoid and teres minor muscles



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over the levator scapulae muscle to innervate the sternocleidomastoid and trapezius muscles.

**(Choice B)** Fracture of the surgical neck of the humerus and anterior dislocation of the glenohumeral joint can cause injury to the axillary nerve. The resultant paralysis of the deltoid and teres minor muscles causes weakness on arm abduction. Sensory loss over the deltoid may also be evident.

**(Choice C)** Damage to the long thoracic nerve causes paralysis of the serratus anterior muscle and winging of the scapula. This nerve is often injured during lymph node dissection in patients undergoing radical mastectomy.

**(Choice D)** Proximal median nerve injury often occurs with supracondylar humerus fractures. This results in sensory loss over the palmar aspect of the first 3 digits and impairment of thumb flexion/opposition, flexion of the second/third digits, and wrist flexion/abduction.

**(Choice F)** The suprascapular nerve innervates the supraspinatus and infraspinatus muscles. These muscles function to abduct and laterally rotate the arm, respectively.

**Educational objective:**
Radial nerve injury can occur with repetitive pressure/trauma at the axilla (eg, improperly fitted crutches). Findings include weakness of the forearm, hand, and fingers extensors (eg, wrist drop, absent triceps reflex) and sensory loss over the posterior arm and forearm, dorsolateral hand, and dorsal thumb. More


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**(Choice C)** Damage to the long thoracic nerve causes paralysis of the serratus anterior muscle and winging of the scapula. This nerve is often injured during lymph node dissection in patients undergoing radical mastectomy.

**(Choice D)** Proximal median nerve injury often occurs with supracondylar humerus fractures. This results in sensory loss over the palmar aspect of the first 3 digits and impairment of thumb flexion/opposition, flexion of the second/third digits, and wrist flexion/abduction.

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**Educational objective:**

Radial nerve injury can occur with repetitive pressure/trauma at the axilla (eg, improperly fitted crutches). Findings include weakness of the forearm, hand, and fingers extensors (eg, wrist drop, absent triceps reflex) and sensory loss over the posterior arm and forearm, dorsolateral hand, and dorsal thumb. More distal lesions spare the triceps brachii.

**References**

- Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical considerations


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A 24-year-old man is being evaluated for a nerve block procedure. The patient has had intermittent burning and stabbing pain in the left groin since undergoing mesh repair of an inguinal hernia a year ago. The pain is often brought on by physical activity and coughing. He has no other medical conditions and takes no medications. Vital signs are within normal limits. On physical examination, there is no weakness of anterior abdominal or lower extremity muscles. Lightly touching the upper medial thigh or upper part of the scrotum elicits burning pain. Cremasteric reflex is normal. The clinical diagnosis is entrapment of a nerve traversing the superficial inguinal ring with the spermatic cord. Blockade of which of the following nerves with a local anesthetic injection is most likely to relieve this patient's symptoms?

- A. Femoral
- B. Genitofemoral
- C. Iliohypogastric
- D. Ilioinguinal
- E. Obturator



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burning and stabbing pain in the left groin since undergoing mesh repair of an inguinal hernia a year ago. The pain is often brought on by physical activity and coughing. He has no other medical conditions and takes no medications. Vital signs are within normal limits. On physical examination, there is no weakness of anterior abdominal or lower extremity muscles. Lightly touching the upper medial thigh or upper part of the scrotum elicits burning pain. Cremasteric reflex is normal. The clinical diagnosis is entrapment of a nerve traversing the superficial inguinal ring with the spermatic cord. Blockade of which of the following nerves with a local anesthetic injection is most likely to relieve this patient's symptoms?

A. Femoral (4%)
B. Genitofemoral (36%)
C. Iliohypogastric (9%)
D. Ilioinguinal (43%)
E. Obturator (6%)

Incorrect
Correct answer

43%

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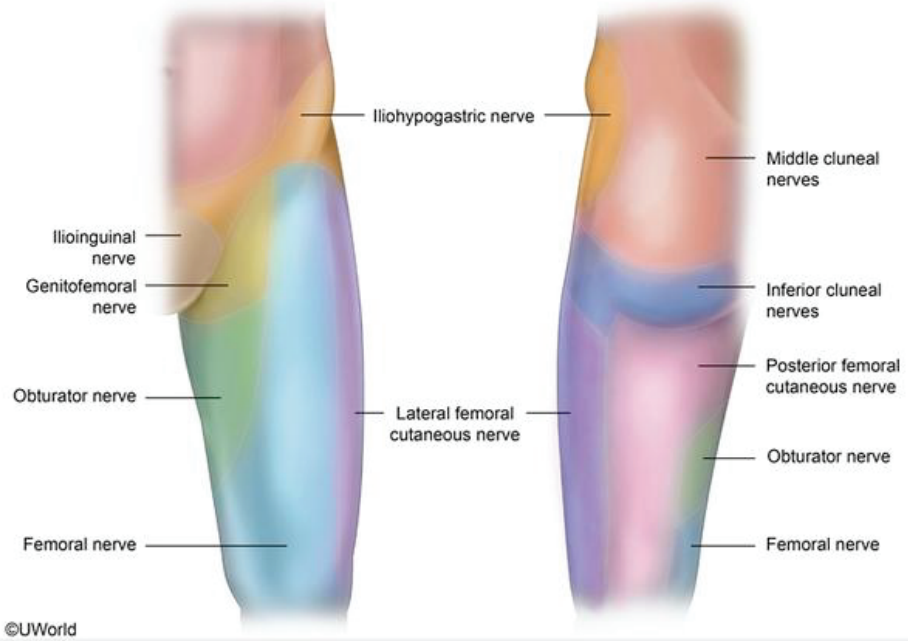
## Abdominopelvic cutaneous innervation

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Inguinal hernia is protrusion of abdominal contents through the abdominal wall above the inguinal ligament, via either the deep/internal inguinal ring and inguinal canal (indirect hernia) or the superficial inguinal ring (direct hernia). Surgical repair involves returning the herniated tissues to the abdomen and closing the defect. Synthetic mesh (eg, polypropylene) is often placed at the site of the defect to reduce tension on the tissues and reduce the risk of recurrence.

**Postherniorrhaphy neuropathy** is a recognized complication of hernia surgery. Regional nerves may be injured during the procedure (eg, transection, cautery) or by postoperative **inflammation and fibrosis** (ie, nerve entrapment).

This patient has a neuropathy of the **ilioinguinal nerve** presenting with **pain and allodynia** (ie, pain caused by normally nonpainful stimuli). The nerve enters the inguinal canal anterior to the internal ring and **follows the spermatic cord** (round ligament in women) to the superficial ring; it gives off sensory branches to:

- **Anterior scrotum** (labia majora)
- **Base of the penis** (mons pubis)



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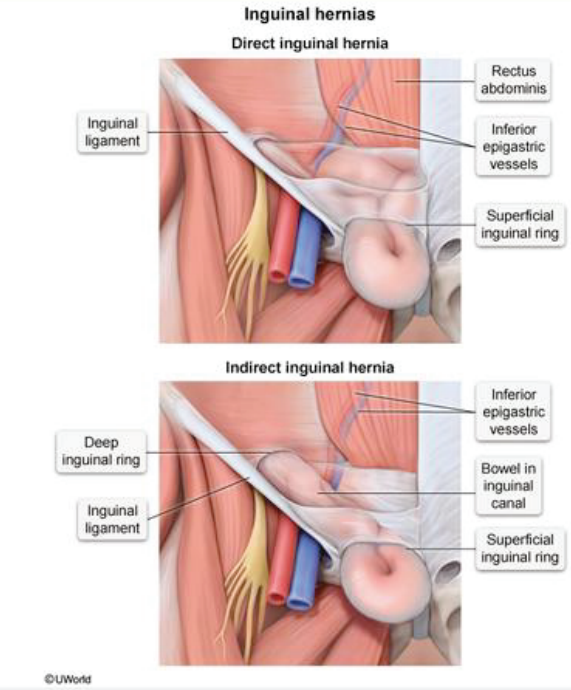


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- **Anterior scrotum** (labia majora)
- **Base of the penis** (mons pubis)
- **Medial thigh**

**(Choice A)** The femoral nerve courses deep to the inguinal ligament; injury during inguinal hernia repair is possible but less common than ilioinguinal injury. Femoral nerve injury causes sensory symptoms in the anterior thigh and motor weakness of the quadriceps.

**(Choice B)** The genital branch of the genitofemoral nerve passes through the inguinal canal; injury may cause pain at the anterior scrotum. However, the cremasteric reflex is mediated primarily by the genitofemoral nerve and is typically diminished when the nerve is injured.

**(Choice C)** The anterior branch of the iliohypogastric nerve is vulnerable to injury where it pierces the anterior abdominal musculature superior to the superficial inguinal ring. However, it does not follow the spermatic cord, and sensory symptoms involve the skin overlying the suprapubic/hypogastric region, not the groin.

**(Choice E)** The obturator nerve innervates the medial compartment of the thigh. Injury presents with weakness of hip adduction and decreased sensation at the medial thigh; it may be injured in pelvic (eg, bladder) surgery but is not at risk in hernia repair.


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**(Choice C)** The anterior branch of the iliohypogastric nerve is vulnerable to injury where it pierces the anterior abdominal musculature superior to the superficial inguinal ring. However, it does not follow the spermatic cord, and sensory symptoms involve the skin overlying the suprapubic/hypogastric region, not the groin.

**(Choice E)** The obturator nerve innervates the medial compartment of the thigh. Injury presents with weakness of hip adduction and decreased sensation at the medial thigh; it may be injured in pelvic (eg, bladder) surgery but is not at risk in hernia repair.

**Educational objective:**
Postherniorrhaphy neuropathy refers to groin pain following hernia repair due to injury involving the cutaneous nerves of the lower abdomen/groin. Neuropathy of the ilioinguinal nerve presents with pain and allodynia in the anterior scrotum (labia majora in women), base of the penis (mons pubis), and medial thigh.

| Anatomy | Nervous System | Groin hernias |
|---|---|---|
| Subject | System | Topic |

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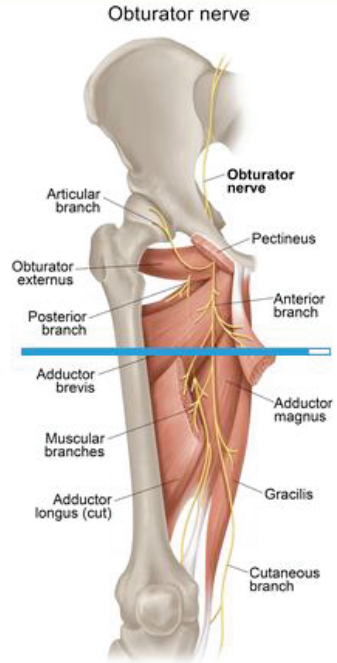


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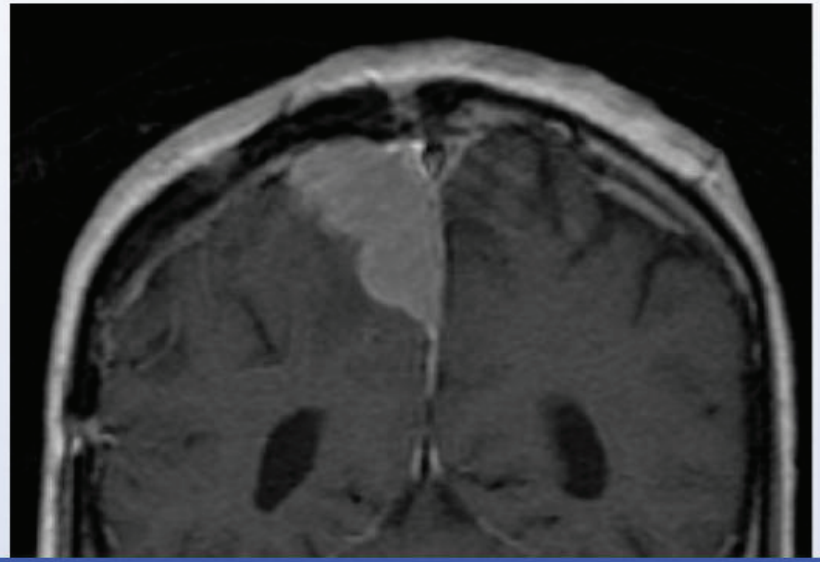
A 43-year-old, right-handed woman is evaluated in the clinic for progressively worsening neurologic symptoms. The patient has a history of diabetes mellitus and hyperlipidemia for which she takes metformin and a statin. She has no history of head trauma or seizures. The patient occasionally drinks wine but does not use tobacco or illicit drugs. Her mother has a history of migraine headaches. A brain MRI is obtained and is shown in the image below:





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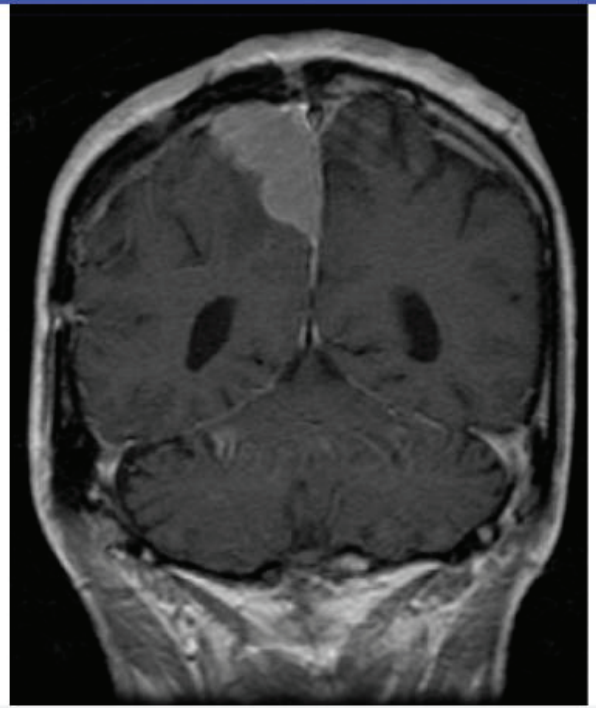

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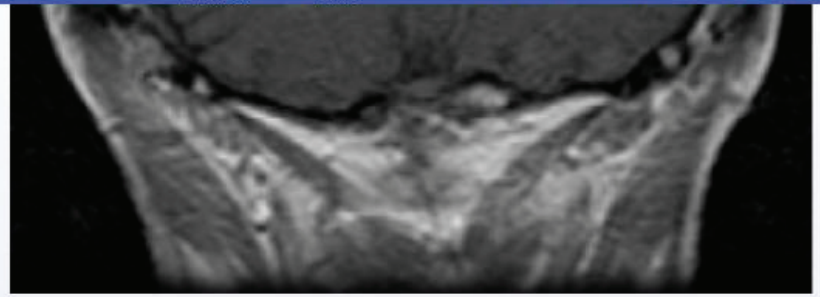

This patient is most likely to have which of the following additional findings?

A. Bitemporal visual field defects

B. Hand weakness and spasticity

C. Lower limb sensory loss and hemineglect

D. Tinnitus and unilateral hearing loss

E. Unilateral ptosis and gaze palsy

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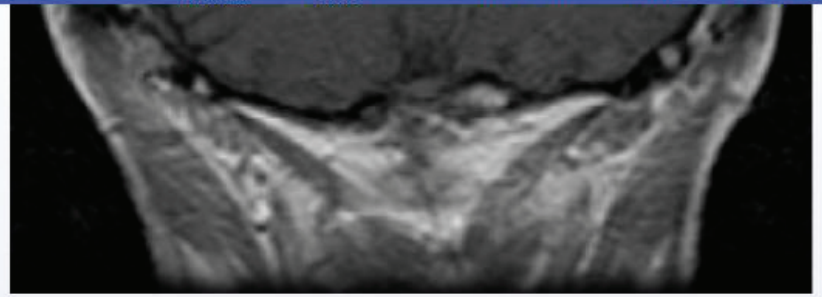

This patient is most likely to have which of the following additional findings?

A. ~~Bitemporal visual field defects~~ (2%)

B. ~~Hand weakness and spasticity~~ (14%)

✓ C. Lower limb sensory loss and hemineglect (78%)

D. Tinnitus and unilateral hearing loss (1%)

E. Unilateral ptosis and gaze palsy (3%)

Correct

78%

44 secs

02/06/2021



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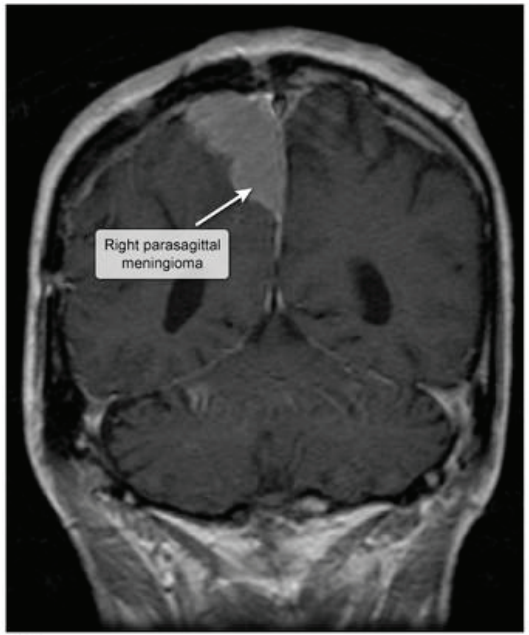
Exhibit Display

Meningioma

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This patient with progressive neurologic symptoms and a well-circumscribed parasagittal tumor most likely has a **meningioma**. Meningiomas are benign, slow-growing intracranial tumors that typically affect adults and tend to arise near **dural reflections** (eg, falx cerebri, tentorium cerebelli). Patients are often asymptomatic but may have headache, seizure, or focal neurologic deficits depending on tumor size and location.

The tumor's parasagittal location compresses the medial portion of the cerebral cortex, which has a somatotopic organization. The medial portion corresponds with the lower extremities, while the lateral portion corresponds with the trunk and upper extremities. This patient's tumor is affecting the medial portion of the postcentral gyrus (primary somatosensory cortex), most likely resulting in **sensory loss** in the **contralateral lower limb**. Involvement of the adjacent parietal association cortex (particularly in the nondominant hemisphere as in this patient) can result in **contralateral hemineglect** due to this region's role in visuospatial processing.

**(Choice A)** Bitemporal hemianopia can occur due to compression of the central portion of the optic chiasm and is commonly caused by pituitary masses or craniopharyngiomas.

**(Choice B)** Hand weakness and spasticity can occur with meningiomas over the lateral convexity compressing the lateral portion of the primary motor cortex in the frontal lobe.



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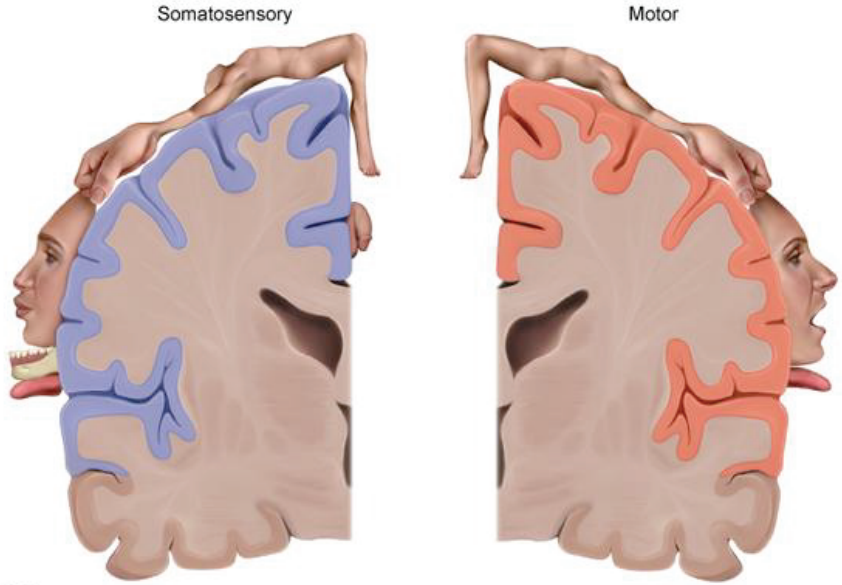
Exhibit Display

**Homunculus**

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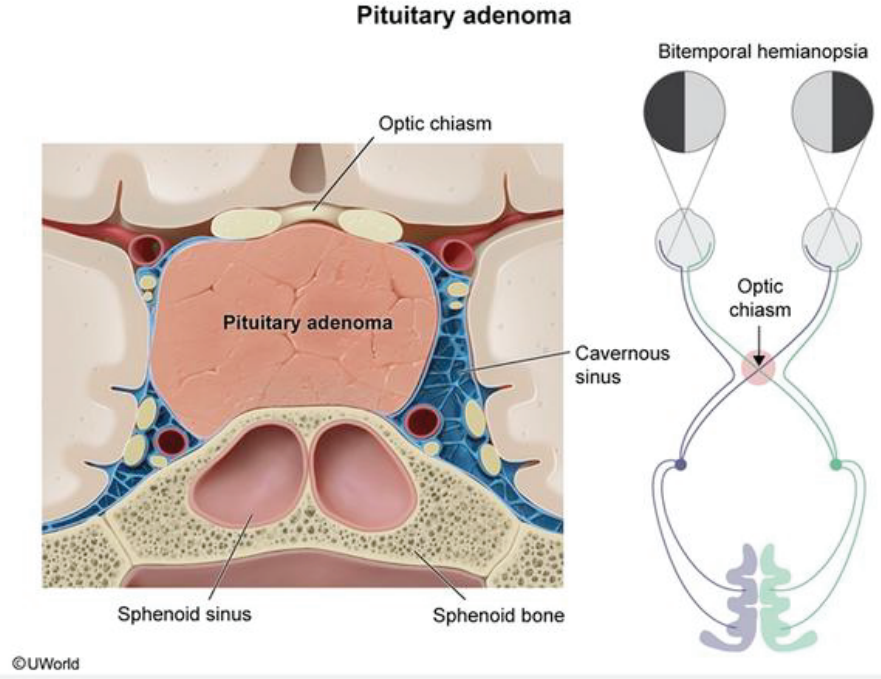


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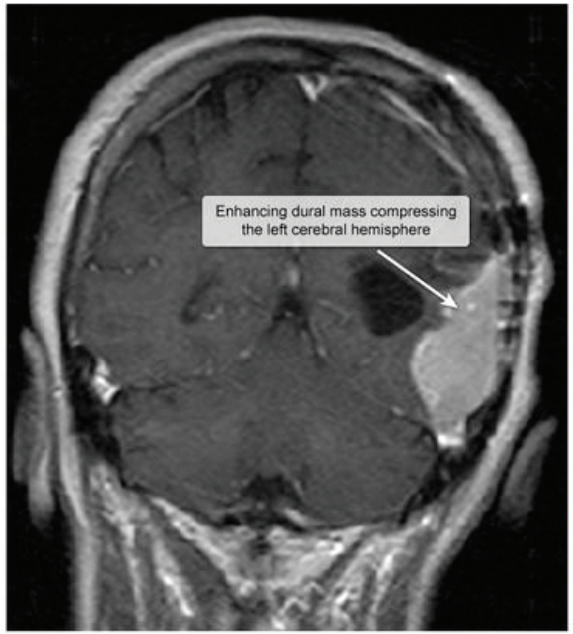
Exhibit Display

Meningioma

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**(Choice B)** Hand weakness and spasticity can occur with meningiomas over the lateral convexity compressing the lateral portion of the primary motor cortex in the frontal lobe.

**(Choice D)** Tinnitus and unilateral hearing loss are common presenting features of vestibular schwannoma, a peripheral nerve tumor characteristically located at the cerebellopontine angle.

**(Choice E)** Unilateral ptosis and gaze palsy ("down and out" gaze) are characteristic of oculomotor nerve palsy, which may occur with nerve damage due to compression (eg, berry aneurysm, uncal herniation) or microvascular ischemia (eg, diabetes mellitus).

**Educational objective:**

Meningiomas are common adult intracranial tumors that typically arise in regions of dural reflection (eg, falx cerebri, tentorium cerebelli). Parasagittal lesions compressing the medial portion of the primary somatosensory cortex in the parietal lobe can result in contralateral lower limb sensory loss along with contralateral hemineglect if there is also damage to the parietal association cortex (nondominant hemisphere).

**References**

- Meningioma.



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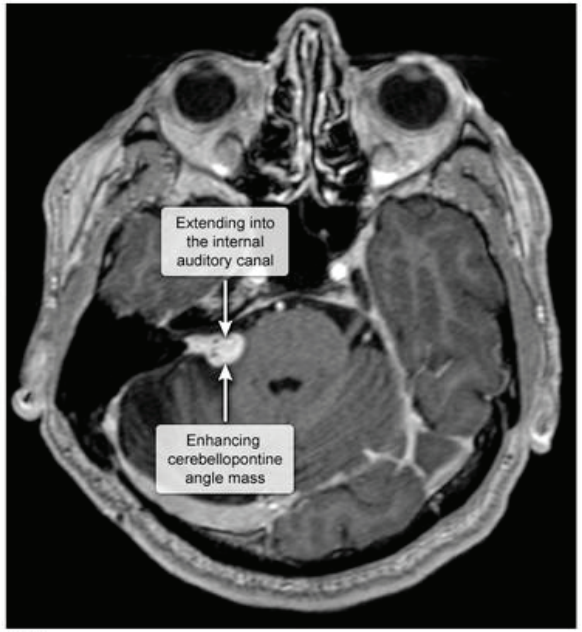
## Exhibit Display

**Acoustic neuroma**

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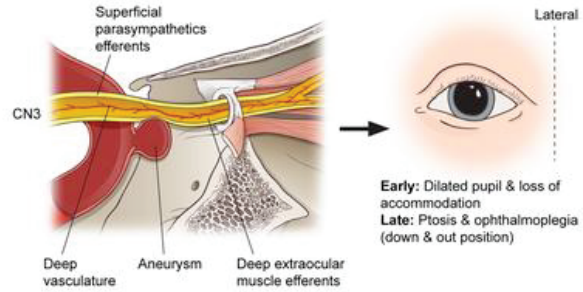
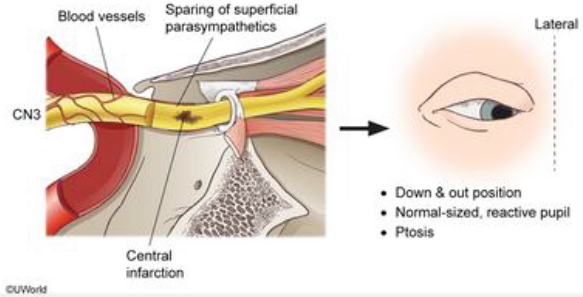
## Exhibit Display

### Aneurysmal compression of oculomotor nerve




### Diabetic ophthalmoplegia

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A 65-year-old woman is brought to the emergency department due to abnormal behavior. The patient was in her usual state of health until 3 hours ago, when she suddenly became confused and kept asking repetitive questions. She has had no headache, abnormal motor activity, or focal weakness or numbness. Medical history is significant for hypertension and migraine. Blood pressure is 136/84 mm Hg and pulse is 80/min. On physical examination, the patient is awake and alert but keeps asking, "What happened?" She can state her date of birth and address correctly, recognizes her family members, and is aware of current events. The patient recalls 0 of 3 objects after several minutes and cannot retain the physician's name despite many repetitions. Speech is fluent without dysarthria or aphasia. Cranial nerve examination shows no abnormalities. Motor strength, reflexes, and sensation are normal throughout. Blood cell count and serum chemistry panel are within normal limits. Urine drug screen is negative. CT scan of the head shows no hemorrhage. Two hours later, the patient spontaneously returns to normal. Temporary dysfunction of which of the following neural structures best explains this patient's symptoms?

A. Arcuate fasciculus

B. Hippocampus

C. Nucleus accumbens



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can state her date of birth and address correctly, recognizes her family members, and is aware of current events. The patient recalls 0 of 3 objects after several minutes and cannot retain the physician's name despite many repetitions. Speech is fluent without dysarthria or aphasia. Cranial nerve examination shows no abnormalities. Motor strength, reflexes, and sensation are normal throughout. Blood cell count and serum chemistry panel are within normal limits. Urine drug screen is negative. CT scan of the head shows no hemorrhage. Two hours later, the patient spontaneously returns to normal. Temporary dysfunction of which of the following neural structures best explains this patient's symptoms?

A. Arcuate fasciculus
B. Hippocampus
C. Nucleus accumbens
D. Piriform cortex
E. Pontine reticular formation

Submit



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can state her date of birth and address correctly, recognizes her family members, and is aware of current events. The patient recalls 0 of 3 objects after several minutes and cannot retain the physician's name despite many repetitions. Speech is fluent without dysarthria or aphasia. Cranial nerve examination shows no abnormalities. Motor strength, reflexes, and sensation are normal throughout. Blood cell count and serum chemistry panel are within normal limits. Urine drug screen is negative. CT scan of the head shows no hemorrhage. Two hours later, the patient spontaneously returns to normal. Temporary dysfunction of which of the following neural structures best explains this patient's symptoms?

A. Arcuate fasciculus (11%)
B. Hippocampus (75%)
C. Nucleus accumbens (5%)
D. Piriform cortex (3%)
E. Pontine reticular formation (4%)

Correct

75%

01 min, 31 secs

11/06/2020



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This patient's sudden-onset confusion, memory loss, and anterograde amnesia (ie, inability to form new memories) resolving within 2 hours is consistent with **transient global amnesia** (TGA). The inability to retain new information during a TGA episode frequently causes patients to ask repetitive questions. In addition to **prominent anterograde amnesia**, patients with TGA have varying degrees of retrograde amnesia (ie, lack of recall of information prior to the episode). They remain fully alert and oriented to self but are typically disoriented to place. Other cognitive functions remain intact during the episode, and neurologic examination is normal. Episodes are self-limited, and **amnestic symptoms resolve fully** (except for events that occurred during the TGA episode itself) within 24 hours by definition.

Risk factors for TGA in this patient include older age and history of migraine. Although the specific etiology of TGA is uncertain, the clinical symptoms and neuroimaging studies implicate dysfunction of the **hippocampus**, the area of the brain critical for formation of new memories.

**(Choice A)** The arcuate fasciculus is an association fiber tract connecting Broca area and Wernicke area in the brain. Dysfunction in this tract correlates with conduction aphasia. Language comprehension and speech are normal in TGA.

**(Choice C)** The nucleus accumbens is part of the basal ganglia. It mediates reward and pleasure and plays an important role in addiction.


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**(Choice A)** The arcuate fasciculus is an association fiber tract connecting Broca area and Wernicke area in the brain. Dysfunction in this tract correlates with conduction aphasia. Language comprehension and speech are normal in TGA.

**(Choice C)** The nucleus accumbens is part of the basal ganglia. It mediates reward and pleasure and plays an important role in addiction.

**(Choice D)** The piriform cortex is the brain region associated with processing olfactory information.

**(Choice E)** The pontine reticular formation is located in the brainstem and regulates arousal, attention, sleep, and muscle tone. Dysfunction in this area is associated with delirium, which is characterized by fluctuating levels of arousal. Patients with TGA are alert and have a relatively isolated deficit of anterograde amnesia.

**Educational objective:**
Transient global amnesia is a self-limited syndrome characterized by the sudden onset of prominent anterograde amnesia accompanied by repetitive questioning. Symptoms correlate with transient dysfunction of the hippocampus, the brain area responsible for the formation of new memories.

**References**

- Transient global amnesia: current perspectives.



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A highly agitated 54-year-old man is brought to the emergency department by his family because he is unable to effectively communicate. He speaks clearly and with conviction but his sentences are incomprehensible. He does not appear to understand the doctor's questions, does not follow oral or written instructions, and cannot repeat simple phrases. Branch occlusion of which of the following arteries is most likely responsible for this patient's condition?

A. Anterior cerebral artery
B. Anterior inferior cerebellar artery
C. Middle cerebral artery
D. Posterior cerebral artery
E. Posterior inferior cerebellar artery

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A highly agitated 54-year-old man is brought to the emergency department by his family because he is unable to effectively communicate. He speaks clearly and with conviction but his sentences are incomprehensible. He does not appear to understand the doctor's questions, does not follow oral or written instructions, and cannot repeat simple phrases. Branch occlusion of which of the following arteries is most likely responsible for this patient's condition?

A. Anterior cerebral artery (4%)
B. Anterior inferior cerebellar artery (1%)
C. Middle cerebral artery (88%)
D. Posterior cerebral artery (4%)
E. Posterior inferior cerebellar artery (1%)

Correct

88%
Answered correctly

43 secs
Time Spent

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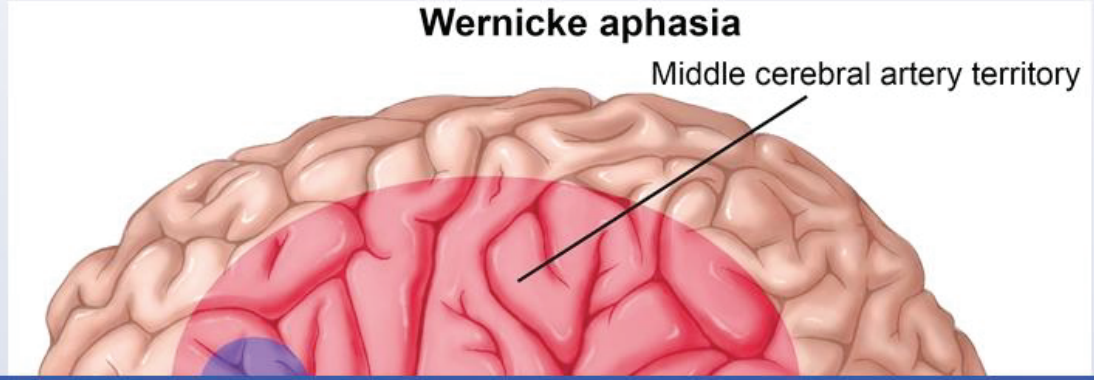
This patient has fluent aphasia, a form of receptive aphasia characterized by speech that is fluent, well articulated, and melodic - but meaningless. Individuals stricken with fluent aphasia cannot understand verbal or written language. Repetition is usually affected to the same degree as the impairment in comprehension. Typically, patients will have no awareness of their cognitive deficit. Fluent aphasia is often produced by a lesion in Wernicke's area, which is located in the auditory association cortex within the posterior portion of the superior temporal gyrus in the dominant (usually left) temporal lobe.

The regions of the cerebral cortex supplied by the middle cerebral artery (MCA) are approximated by the red oval in the image below. The inferior terminal MCA branches supply Wernicke's area.



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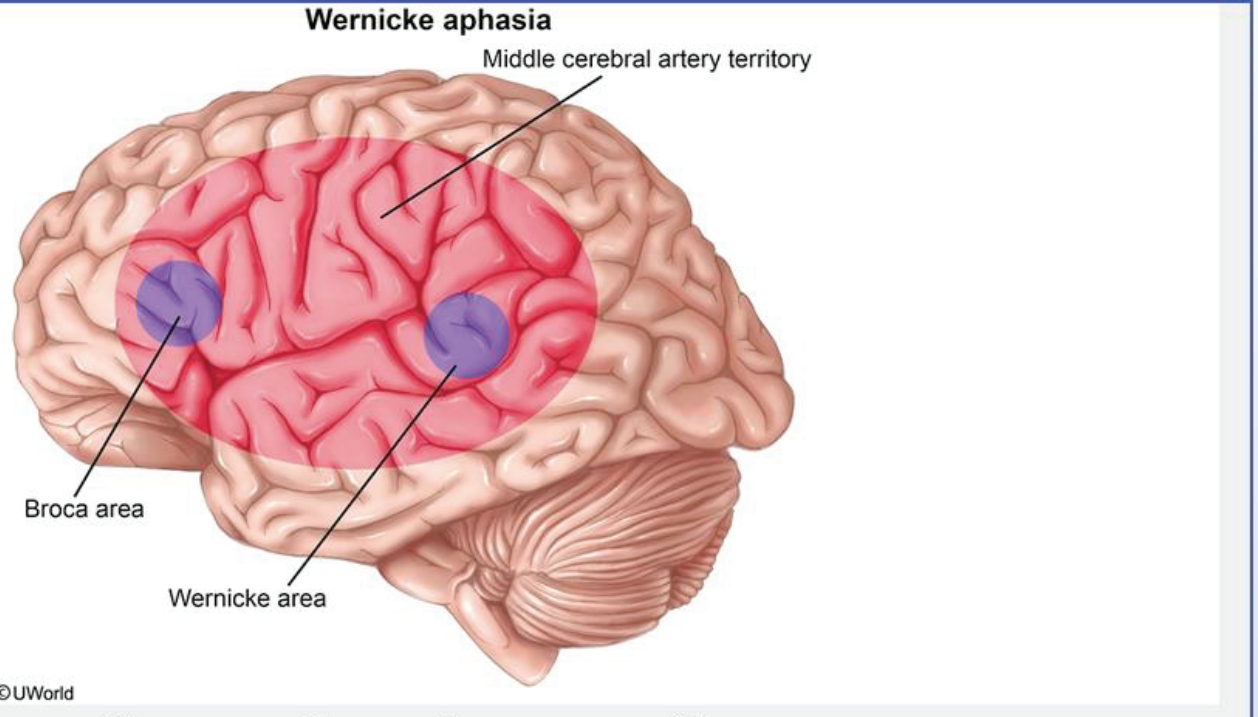


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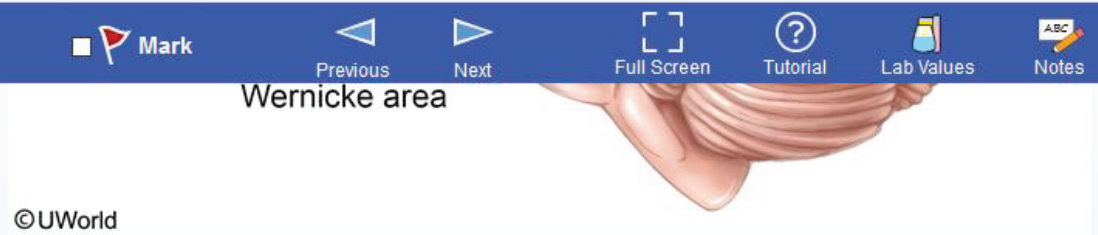


**(Choices A, B, D, and E)** The anterior cerebral artery, anterior inferior cerebellar artery, posterior cerebral artery, and posterior inferior cerebellar artery do not typically service Wernicke's area. Consequently, occlusions of these arteries would not be associated with Wernicke's aphasia.

**Educational objective:**

A lesion in Wernicke's area can cause receptive aphasia, which is characterized by well-articulated, nonsensical speech paired with a lack of language comprehension (**W**ernicke-**W**ord salad). Wernicke's area is located in the auditory association cortex within the posterior portion of the superior temporal gyrus in the dominant temporal lobe. The middle cerebral artery supplies Broca's area (superior division) and Wernicke's area (inferior division).

| Anatomy | Nervous System | Aphasia |
|---|---|---|
| Subject | System | Topic |

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A 34-year-old woman is evaluated for several months of moderate hearing loss. She has also noticed a ringing in her left ear. The patient has had no recent ear infections or cold symptoms, does not use cotton ear swabs, and has no history of head trauma. Her father has bilateral hearing loss attributed to old age. On physical examination, the auditory canals are patent and tympanic membranes appear gray with a well-visualized light reflex. Hearing is diminished on the left side. Neurologic examination shows left-sided facial numbness, an asymmetric smile, and diminished corneal reflex response in the left eye. This patient's condition suggests an intracranial mass in which of the following locations?

A. Above the sellar diaphragm
B. Adjacent to the sagittal sinus
C. Between the cerebellum and lateral pons
D. In the dorsal midbrain
E. Over the lateral cerebral convexity

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A. Above the sellar diaphragm (2%)
B. ~~Adjacent to the sagittal sinus~~ (4%)
✓ C. Between the cerebellum and lateral pons (78%)
D. ~~In the dorsal midbrain~~ (9%)
E. ~~Over the lateral cerebral convexity~~ (4%)

78%  01 min, 40 secs  02/06/2021



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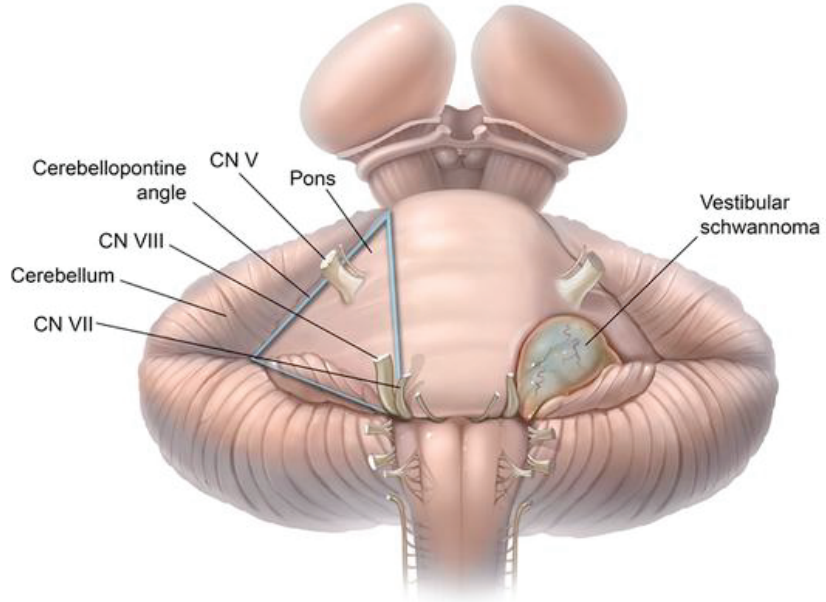
Exhibit Display

## Cerebellopontine angle with vestibular schwannoma

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Anterior view

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**Anterior view**

This patient's unilateral hearing loss with associated facial numbness and weakness, is highly suggestive of a **vestibular schwannoma**, the most common cause of cerebellopontine angle (ie, between the cerebellum and lateral pons) tumors in adults. Vestibular schwannomas most often arise from the vestibular portion of the vestibulocochlear nerve (CN VIII). Spontaneous vestibular schwannomas are usually unilateral, whereas bilateral vestibular schwannomas are associated with neurofibromatosis type 2.

The facial nerve (CN VII) and trigeminal nerve (CN V) are in proximity to CN VIII at the cerebellopontine angle and may be compressed by vestibular schwannomas. Symptoms can vary based on the pattern of nerve involvement:

- Impairment of the cochlear portion of CN VIII leads to ipsilateral **sensorineural hearing loss** and **tinnitus** (ringing in the ear), and damage to the vestibular portion causes unsteadiness and **disequilibrium**.
- Compression of CN V may cause loss of ipsilateral facial sensation with interruption of the afferent limb of the corneal reflex.
- CN VII compression can result in ipsilateral facial muscle paralysis (eg, asymmetric smile).



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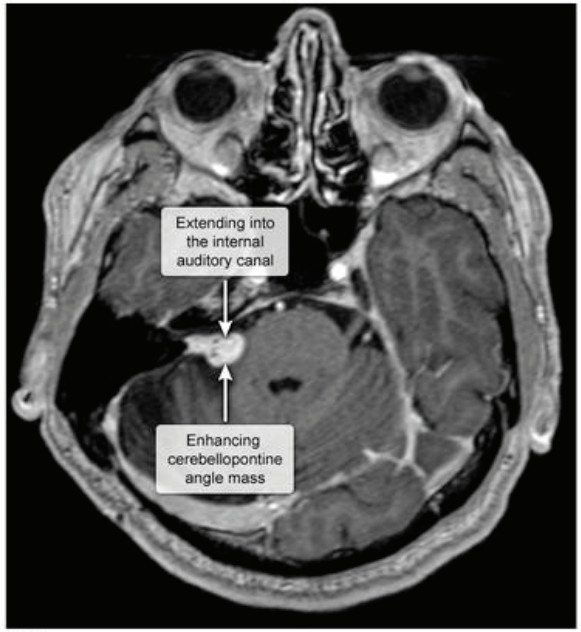
Exhibit Display

Acoustic neuroma

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of the corneal reflex.

- CN VII compression can result in ipsilateral facial muscle paralysis (eg, asymmetric smile).

**(Choice A)** Craniopharyngiomas arise from remnants of Rathke's pouch and are typically located in the suprasellar region. Patients usually have hypothalamic or pituitary dysfunction and changes in vision due to disruption of the optic chiasm (eg, bitemporal hemianopia), none of which are evident in this patient.

**(Choices B and E)** Meningiomas are most commonly found in the falcine/parasagittal region or over the convexities of the cerebral hemispheres. Most are discovered incidentally, but some patients may have seizures, headaches, or focal neurologic deficits. This patient's findings are localized to CN V, CN VII, and CN VIII, making vestibular schwannoma more likely.

**(Choice D)** Germ cell tumors frequently arise from the pineal gland in the dorsal midbrain. Pineal tumors can cause obstructive hydrocephalus with symptoms of increased intracranial pressure (eg, headache, vomiting, altered mental status) and Parinaud syndrome (eg, upward gaze palsy).

**Educational objective:**
Vestibular schwannomas arise from the vestibulocochlear nerve (CN VIII) and are usually located at the cerebellopontine angle. These tumors can cause a range of symptoms by damaging the vestibulocochlear


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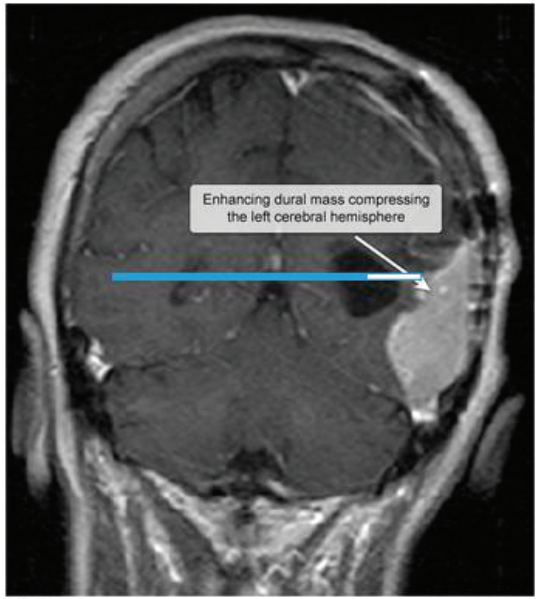
## Exhibit Display

Meningioma Para-falcine meningioma

**Meningioma**

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## Exhibit Display

Meningioma Para-falcine meningioma

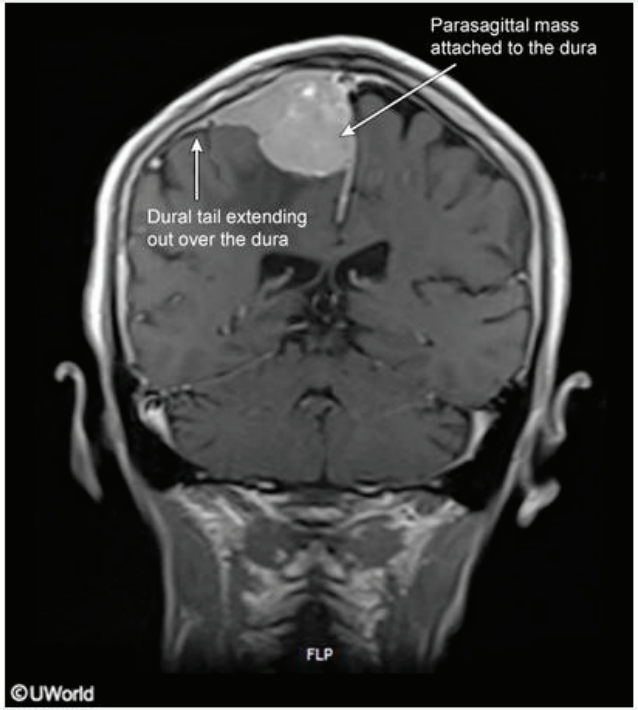


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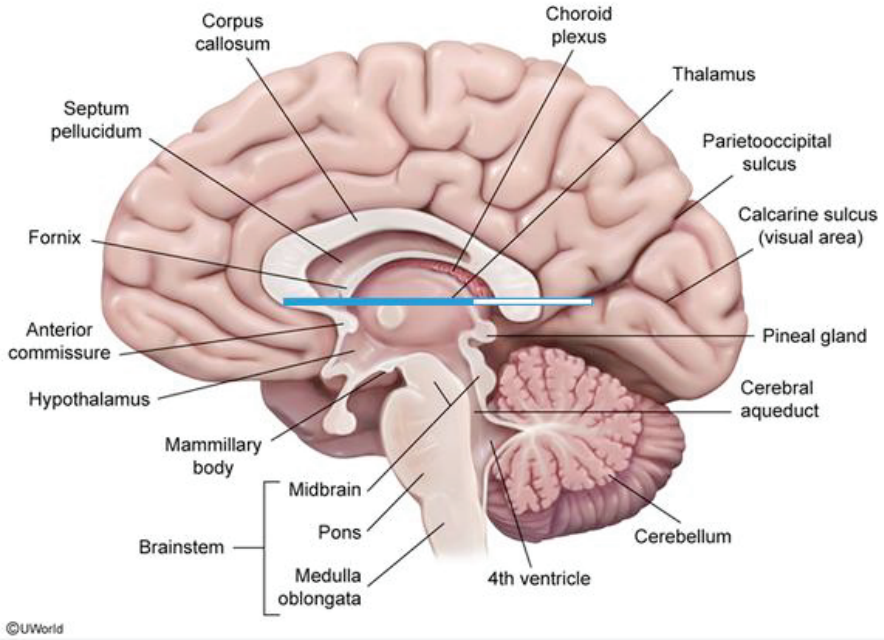
Exhibit Display

Median brain

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suprasellar region. Patients usually have hypothalamic or pituitary dysfunction and changes in vision due to disruption of the optic chiasm (eg, bitemporal hemianopia), none of which are evident in this patient.

**(Choices B and E)** Meningiomas are most commonly found in the falcine/parasagittal region or over the convexities of the cerebral hemispheres. Most are discovered incidentally, but some patients may have seizures, headaches, or focal neurologic deficits. This patient's findings are localized to CN V, CN VII, and CN VIII, making vestibular schwannoma more likely.

**(Choice D)** Germ cell tumors frequently arise from the pineal gland in the dorsal midbrain. Pineal tumors can cause obstructive hydrocephalus with symptoms of increased intracranial pressure (eg, headache, vomiting, altered mental status) and Parinaud syndrome (eg, upward gaze palsy).

**Educational objective:**

Vestibular schwannomas arise from the vestibulocochlear nerve (CN VIII) and are usually located at the cerebellopontine angle. These tumors can cause a range of symptoms by damaging the vestibulocochlear nerve (unsteadiness and ipsilateral sensorineural hearing loss with tinnitus), trigeminal nerve (ipsilateral facial paresthesia and diminished corneal reflex), and facial nerve (ipsilateral facial paresis). Bilateral acoustic neuromas are associated with neurofibromatosis type 2.

**References**



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order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 62-year-old woman comes to the emergency department due to difficulty walking that started 3 hours ago. The patient cannot feel the right side of her body. She has a history of hypertension and diabetes mellitus. She has smoked a pack of cigarettes daily for the past 30 years. The patient's father had a myocardial infarction at age 60. Physical examination shows loss of touch, temperature, and vibratory sensation affecting the right upper and lower extremities. Sensation is also diminished over the right side of the face. Muscle strength is 5/5 throughout.

**Item 1 of 2**

This patient has most likely suffered a stroke affecting which of the following brain structures?

A. Base of the pons
B. Caudate nucleus
C. Frontal cortex
D. Posterior limb of the internal capsule
E. Ventral posterior thalamus


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A 62-year-old woman comes to the emergency department due to difficulty walking that started 5 hours ago. The patient cannot feel the right side of her body. She has a history of hypertension and diabetes mellitus. She has smoked a pack of cigarettes daily for the past 30 years. The patient's father had a myocardial infarction at age 60. Physical examination shows loss of touch, temperature, and vibratory sensation affecting the right upper and lower extremities. Sensation is also diminished over the right side of the face. Muscle strength is 5/5 throughout.

**Item 1 of 2**

This patient has most likely suffered a stroke affecting which of the following brain structures?

A. Base of the pons (11%)
B. ~~Caudate nucleus~~ (3%)
C. ~~Frontal cortex~~ (5%)
D. Posterior limb of the internal capsule (28%)
E. Ventral posterior thalamus (50%)


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This patient with right-sided pure hemisensory loss has likely suffered from a **thalamic stroke**. The thalamic **ventral posterior lateral nucleus** (receives input from the spinothalamic tract and dorsal columns) and **ventral posterior medial nucleus** (receives input from the trigeminal pathway) send somatosensory projections to the cortex via thalamocortical fibers. Damage to these nuclei (eg, due to ischemia, hemorrhage) may result in **complete contralateral sensory loss** (eg, touch, pain/temperature, vibration/proprioception). Severe proprioceptive defects may cause **unsteady gait**.

**(Choice A)** Injury to the base of the pons is frequently associated with contralateral weakness and ataxia due to involvement of the descending motor tracts (eg, corticospinal, corticobulbar) and pontocerebellar fibers.

**(Choice B)** Damage to the caudate nucleus typically causes behavioral abnormalities (eg, agitation, psychosis, abulia), speech/language disturbances, and movement disorders (eg, choreoathetosis).

**(Choice C)** Frontal cortex lesions usually cause social disinhibition and deficits in attention and executive function (eg, planning, organizing, decision making).

**(Choice D)** The anterior two-thirds of the posterior limb of the internal capsule is mainly composed of motor fibers (eg, corticospinal tract), and the posterior one-third contains sensory fibers (eg, thalamocortical


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**(Choice B)** Damage to the caudate nucleus typically causes behavioral abnormalities (eg, agitation, psychosis, abulia), speech/language disturbances, and movement disorders (eg, choreoathetosis).

**(Choice C)** Frontal cortex lesions usually cause social disinhibition and deficits in attention and executive function (eg, planning, organizing, decision making).

**(Choice D)** The anterior two-thirds of the posterior limb of the internal capsule is mainly composed of motor fibers (eg, corticospinal tract), and the posterior one-third contains sensory fibers (eg, thalamocortical tract). Although very small lesions to the posterior limb may cause contralateral pure sensory deficits, most lesions result in pure motor or combined sensorimotor deficits.

**Educational objective:**

The ventral posterior lateral nucleus (receives input from the spinothalamic tract and dorsal columns) and ventral posterior medial nucleus (receives input from the trigeminal pathway) of the thalamus send somatosensory projections to the cortex via thalamocortical fibers. Damage to these nuclei results in complete contralateral sensory loss.

**References**

- Pure sensory stroke. Clinical-radiological correlates of 21 cases.



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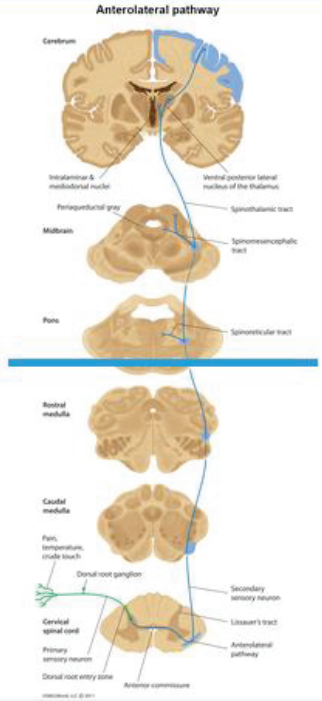


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function (eg, planning, organizing, decision making).



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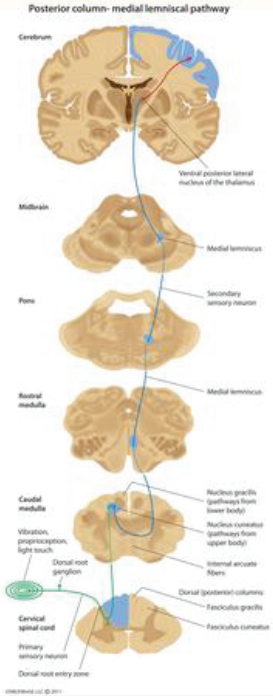


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function (eg, planning, organizing, decision making).



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## Item 2 of 2

The patient was diagnosed with a pure sensory stroke and received the appropriate treatment. Her symptoms improved and she returned home to live with her daughter after a few weeks of physical rehabilitation. Five years later, the patient dies of a large myocardial infarction. On autopsy, there are two 5- to 6-mm cavities in the deep structures of her brain filled with clear fluid. Which of the following processes was most likely responsible for the patient's brain findings?

A. Autoimmune demyelination
B. Embolic carotid atherosclerosis
C. Embolic mitral valve disease
D. Lipohyalinosis with small vessel occlusion
E. Malignant cell infiltration

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## Item 2 of 2

The patient was diagnosed with a pure sensory stroke and received the appropriate treatment. Her symptoms improved and she returned home to live with her daughter after a few weeks of physical rehabilitation. Five years later, the patient dies of a large myocardial infarction. On autopsy, there are two 5- to 6-mm cavities in the deep structures of her brain filled with clear fluid. Which of the following processes was most likely responsible for the patient's brain findings?

A. Autoimmune demyelination (3%)
B. Embolic carotid atherosclerosis (23%)
C. Embolic mitral valve disease (7%)
D. Lipohyalinosis with small vessel occlusion (62%)
E. Malignant cell infiltration (3%)

Correct

62%
Answered correctly

46 secs
Time Spent

12/08/2020
Last Updated



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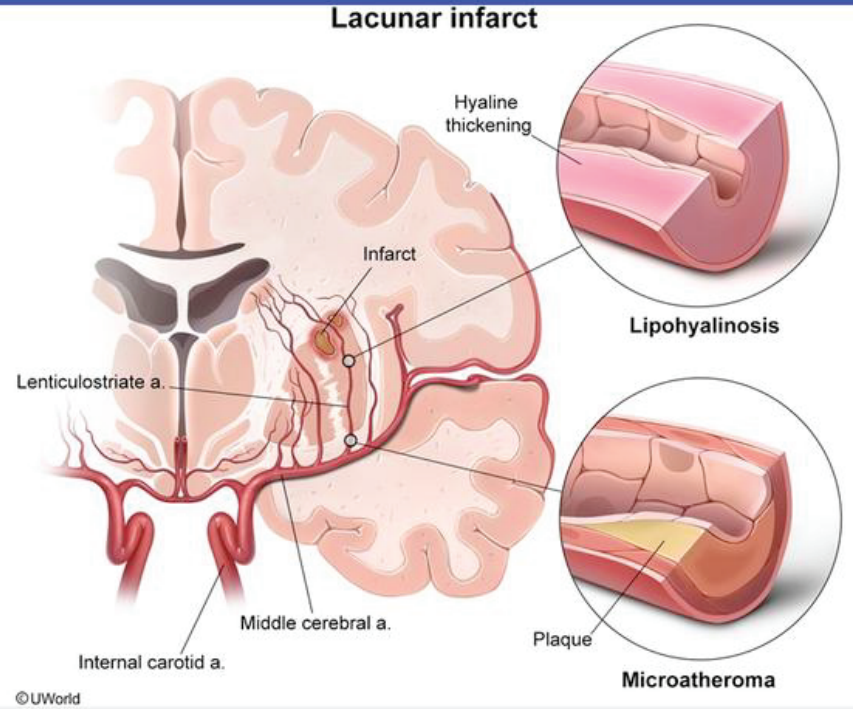


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Plaque



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**Lacunes** are small (<15 mm) cavitary infarcts located within the basal ganglia, posterior limb of the internal capsule, pons, and cerebellum. The infarcts result from occlusion of the **small penetrating arteries** that supply these deep brain structures (eg, lenticulostriate arteries), most commonly in the setting of chronic uncontrolled **hypertension** or **diabetes mellitus**.

Lipohyalinosis and microatheromas are believed to be the primary causes of lacunar infarcts. **Lipohyalinosis** occurs secondary to leakage of plasma proteins through damaged endothelium and is characterized by hyaline thickening of the vascular wall, collagenous sclerosis, and accumulation of mural foamy macrophages. **Microatheromas** result from atherosclerotic accumulation of lipid-laden macrophages within the intimal layer of a penetrating artery near its origin off the parent vessel. These changes predispose to small-vessel **occlusion** and infarction of central nervous system (CNS) tissue with **liquefactive necrosis** and the formation of a fluid-filled cavity.

**(Choice A)** Multiple sclerosis is an autoimmune demyelinating disease of the CNS. The CNS lesions in multiple sclerosis do not form cavities; instead, they appear grossly as pink patches in the white matter tracts.

**(Choices B and C)** Embolism due to carotid atherosclerosis and mitral valve disease (eg, bacterial endocarditis) most commonly causes cortical infarcts. Although microemboli released from atherosclerotic



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tracts.

**(Choices B and C)** Embolism due to carotid atherosclerosis and mitral valve disease (eg, bacterial endocarditis) most commonly causes cortical infarcts. Although microemboli released from atherosclerotic lesions or valvular disease may be the cause of some lacunar infarcts, lipohyalinosis/microatheromas are a much more common etiology.

**(Choice E)** Malignant neoplasms tend to cause space-occupying lesions rather than small cavities. The center of a large tumor may cavitate due to insufficient perfusion, with resultant necrosis and hemorrhage.

**Educational objective:**
Lacunar infarctions are the result of small vessel occlusion (eg, due to lipohyalinosis and microatheroma formation) in the penetrating vessels supplying the deep brain structures. Uncontrolled hypertension and diabetes mellitus are major risk factors for this condition.

**References**

- Lacunar infarction and small vessel disease: pathology and pathophysiology.

| Anatomy | Nervous System | Ischemic stroke |
|---|---|---|
| Subject | System | Topic |



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www.ncbi.nlm.nih.gov/pubmed/25692102

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A 66-year-old man develops transient, painless vision loss in the left eye. He has a history of hypertension, hyperlipidemia, and type 2 diabetes mellitus. Evaluation reveals significant stenosis of the left internal carotid artery due to atherosclerotic plaque. Carotid endarterectomy is performed. During the surgery, the left glossopharyngeal nerve is accidentally transected. Which of the following is most likely to be seen due to the nerve injury?

A. Deviation of the protruded tongue toward the left

B. Hoarseness due to left vocal cord dysfunction

C. Impaired taste sensation from the anterior two-thirds of the tongue

D. Loss of general sensation at the tonsillar lining

E. Reduced salivary secretion from the submandibular gland

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A 66-year-old man develops transient, painless vision loss in the left eye. He has a history of hypertension, hyperlipidemia, and type 2 diabetes mellitus. Evaluation reveals significant stenosis of the left internal carotid artery due to atherosclerotic plaque. Carotid endarterectomy is performed. During the surgery, the left glossopharyngeal nerve is accidentally transected. Which of the following is most likely to be seen due to the nerve injury?

- A. Deviation of the protruded tongue toward the left (17%)
- B. ~~Hoarseness due to left vocal cord dysfunction~~ (9%)
- C. ~~Impaired taste sensation from the anterior two-thirds of the tongue~~ (6%)
- D. Loss of general sensation at the tonsillar lining (56%)
- E. ~~Reduced salivary secretion from the submandibular gland~~ (9%)

Incorrect
Correct answer
D

56%
Answered correctly

01 min, 37 secs
Time Spent

09/12/2020
Last Updated



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The **glossopharyngeal nerve**, or cranial nerve (CN) IX, originates in the medulla and exits the cranial cavity via the jugular foramen. This nerve has numerous functions, including:

- Somatic motor: Stylopharyngeus muscle only (elevates larynx during swallowing)
- Parasympathetic: Inferior salivatory nucleus → CN IX → otic ganglion → travels along auriculotemporal nerve (CN V) → parotid gland secretion
- General sensory: Tympanic membrane (inner surface), eustachian tube, posterior third of tongue, tonsillar region, upper pharynx (afferent portion of gag reflex), carotid body, and carotid sinus
- Special sensory (taste): Posterior third of tongue

Glossopharyngeal nerve lesions therefore result in loss of the **gag reflex** (afferent limb); loss of general sensation in the upper pharynx, posterior tongue, **tonsils**, and middle ear cavity; and loss of **taste** sensation on the **posterior** third of the tongue.

**(Choice A)** Protrusion of the tongue is mediated by motor efferent fibers carried by the hypoglossal nerve (CN XII).

**(Choice B)** The muscles of the larynx are innervated predominantly by the vagus nerve and its branches (particularly the recurrent laryngeal nerve).



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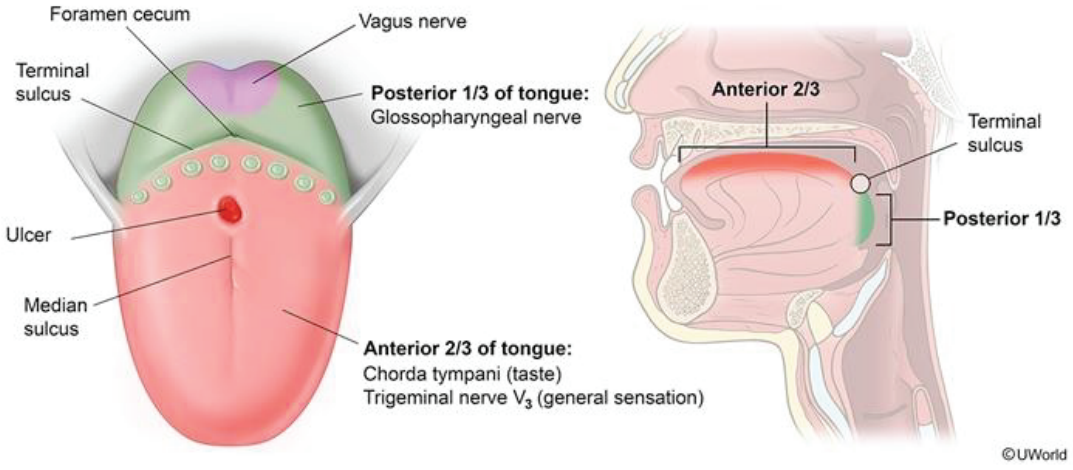
## Tongue sensory innervation

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**(Choice A)** Protrusion of the tongue is mediated by motor efferent fibers carried by the hypoglossal nerve (CN XII).

**(Choice B)** The muscles of the larynx are innervated predominantly by the vagus nerve and its branches (particularly the recurrent laryngeal nerve).

**(Choice C)** Taste sensation from the anterior two-thirds of the tongue is mediated by the chorda tympani branch of the facial nerve (CN VII).

**(Choice E)** Salivary secretion from the submandibular and sublingual glands is mediated by parasympathetic fibers originating in the superior salivatory nucleus carried on the facial nerve (CN VII) via the chorda tympani and lingual nerves across the submandibular ganglion.

**Educational objective:**
Lesions of the glossopharyngeal nerve result in loss of the gag reflex (afferent limb); loss of sensation in the upper pharynx, posterior tongue, tonsils, and middle ear cavity; and loss of taste sensation on the posterior third of the tongue.

| Anatomy | Nervous System | Cranial nerve palsy |
|---|---|---|
| Subject | System | Topic |



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A 9-year old girl is brought to the emergency department by her parents due to severe headache, lethargy, and vomiting. Her symptoms began a few weeks ago with mild intermittent headaches and fatigue and have progressively worsened. A CT scan of the brain reveals a mass lesion, enlarged lateral and third ventricles, and a normal-sized fourth ventricle. Which of the following is the most likely site of obstruction in this patient?

A. Arachnoid Villi
B. Cerebral aqueduct
C. Interventricular foramina of Monro
D. Lateral foramina of Luschka
E. Medial foramen of Magendie

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A 9-year old girl is brought to the emergency department by her parents due to severe headache, lethargy, and vomiting. Her symptoms began a few weeks ago with mild intermittent headaches and fatigue and have progressively worsened. A CT scan of the brain reveals a mass lesion, enlarged lateral and third ventricles, and a normal-sized fourth ventricle. Which of the following is the most likely site of obstruction in this patient?

A. Arachnoid Villi (0%)
B. Cerebral aqueduct (81%)
C. Interventricular foramina of Monro (13%)
D. Lateral foramina of Luschka (2%)
E. Medial foramen of Magendie (2%)

Correct

81%
Answered correctly

33 secs
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01/01/2021
Last Updated



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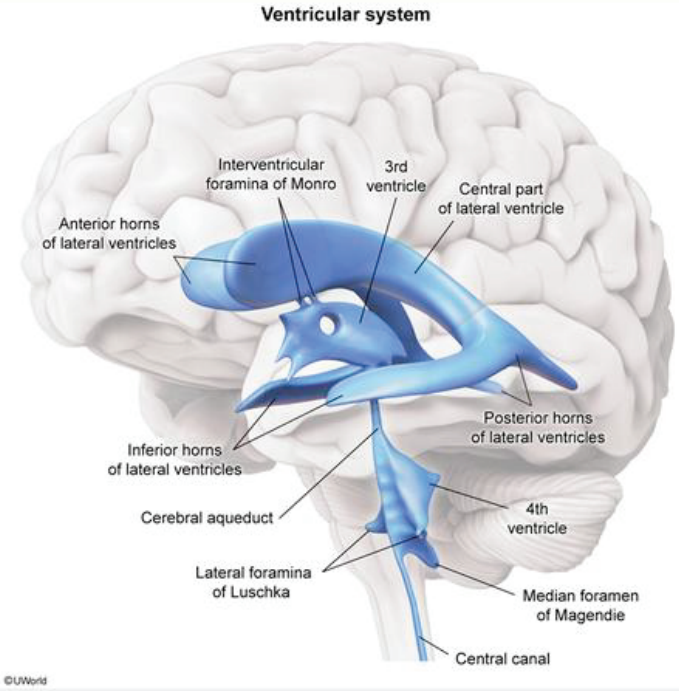


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Cerebrospinal fluid (CSF) is formed by 4 choroid plexuses found in each of the ventricles. The choroid plexus is composed of ependymal cell-covered outgrowths of pia mater capillaries that are fenestrated unlike other central nervous system (CNS) capillaries. The ependymal layer is a simple ciliated columnar epithelium with tight junctions between the cells. This selectively allows only certain materials from the blood to enter the CSF. Once formed, CSF flows from the lateral ventricles to the third ventricle via the interventricular foramina of Monro. It then circulates to the fourth ventricle through the cerebral aqueduct (of Sylvius). CSF then exits the fourth ventricle and enters the subarachnoid space via one of 3 foramina: the 2 lateral foramina of Luschka and the single midline foramen of Magendie. CSF is returned to the venous circulation via the arachnoid villi (granulations).

This patient has findings consistent with noncommunicating (obstructive) hydrocephalus. Obstruction of CSF flow is most commonly caused by tumors, scarring (post-hemorrhage, infection), and CNS malformations. In this patient, obstruction at the level of the cerebral aqueduct causes increased pressures and ventricular dilation proximal to the site of blockage, which includes the lateral and third ventricles. The fourth ventricle is normal-sized as it is distal to the obstruction. In contrast, obstruction at the foramen of Magendie and Luschka would cause enlargement of all 4 ventricles **(Choices D and E)**, while obstruction at the foramen of Monro would cause enlargement of only the affected lateral ventricle **(Choice C)**.



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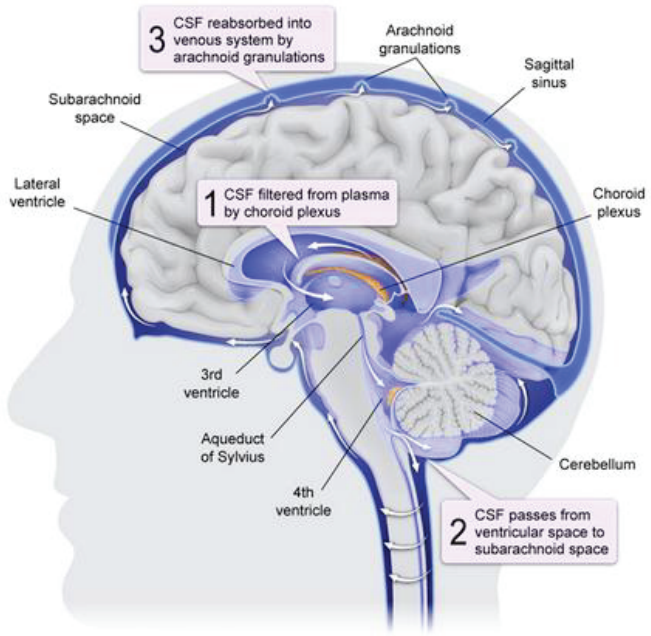
## Exhibit Display

### Flow of cerebrospinal fluid




CSF = cerebrospinal fluid.

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fourth ventricle is normal-sized as it is distal to the obstruction. In contrast, obstruction at the foramen of Magendie and Luschka would cause enlargement of all 4 ventricles **(Choices D and E)**, while obstruction at the foramen of Monro would cause enlargement of only the affected lateral ventricle **(Choice C)**.

Other forms of hydrocephalus are described below:

1. **Communicating hydrocephalus** presents with global ventricular dilation and increased intracranial pressure (ICP) without significant blockage to CSF flow within the brain or brainstem. It usually results from impaired CSF absorption by the arachnoid villi due to inflammation and fibrosis caused by hemorrhage or infection **(Choice A)**. It rarely occurs due to increased production of CSF caused by papillomas of the choroid plexus.

2. **Normal pressure hydrocephalus** presents with enlarged ventricles in the setting of normal ICP. It is considered to be a form of communicating hydrocephalus where impaired absorption of CSF is compensated for by decreased CSF formation. Although ICP is normal, there is still a pressure gradient between the ventricles and subarachnoid space which is responsible for the ventricular enlargement. Communicating hydrocephalus is more often found in infants and children, while normal pressure hydrocephalus is most commonly found in adults.

3. **Hydrocephalus ex vacuo** presents with normal ICP and increased dilatation of ventricles secondary to cortical atrophy. It occurs most often in elderly patients with dementia.



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gradient between the ventricles and subarachnoid space which is responsible for the ventricular enlargement. Communicating hydrocephalus is more often found in infants and children, while normal pressure hydrocephalus is most commonly found in adults.

3. **Hydrocephalus ex vacuo** presents with normal ICP and increased dilatation of ventricles secondary to cortical atrophy. It occurs most often in elderly patients with dementia.

4. **Pseudotumor cerebri** presents with elevated ICP and classically occurs in young women who are overweight. The etiology of the condition is not well known, but it is thought to be related to cerebral venous outflow abnormalities due to elevated intracranial pressures.

**Educational objective:**

CSF flows from the third ventricle to the fourth ventricle via the cerebral aqueduct of Sylvius. Obstruction at this level can cause dilated lateral and third ventricles with a normal-sized fourth ventricle. Obstruction at the foramen of Monro would cause enlargement of only the affected lateral ventricle, while obstruction at the foramen of Magendie and Luschka causes enlargement of all 4 ventricles.

| Anatomy | Nervous System | Hydrocephalus |
|---|---|---|
| Subject | System | Topic |



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A 56-year-old man comes to the office for evaluation of right leg pain and numbness. The pain started 2 days ago during an 8-hour car ride during which the patient was a backseat passenger in a small car. Midway through the car ride, he began to have numbness and burning pain over the lateral aspect of the right thigh. The patient has tried stretching to relieve the pain, but it has only worsened and he is now unable to wear a belt due to the discomfort. He has type 2 diabetes mellitus and has gained 11.3 kg (25 lb) over the past year. BMI is 42 kg/m$^2$. On examination, lower extremity strength is 5/5 bilaterally. The right leg has a large area of numbness over the upper lateral thigh. Straight leg raise is negative. Reflexes are symmetrical and intact. Compression of which of the following nerves is the most likely cause of this patient's presentation?

A. Ilioinguinal
B. Lateral femoral cutaneous
C. Obturator
D. Pelvic splanchnic
E. Sciatic



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Midway through the car ride, he began to have numbness and burning pain over the lateral aspect of the right thigh. The patient has tried stretching to relieve the pain, but it has only worsened and he is now unable to wear a belt due to the discomfort. He has type 2 diabetes mellitus and has gained 11.3 kg (25 lb) over the past year. BMI is 42 kg/m$^2$. On examination, lower extremity strength is 5/5 bilaterally. The right leg has a large area of numbness over the upper lateral thigh. Straight leg raise is negative. Reflexes are symmetrical and intact. Compression of which of the following nerves is the most likely cause of this patient's presentation?

- A. ~~Ilioinguinal~~ (2%)
- ✓ B. Lateral femoral cutaneous (88%)
- C. Obturator (3%)
- D. Pelvic splanchnic (0%)
- E. ~~Sciatic~~ (5%)

Correct

88%

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01/09/2021



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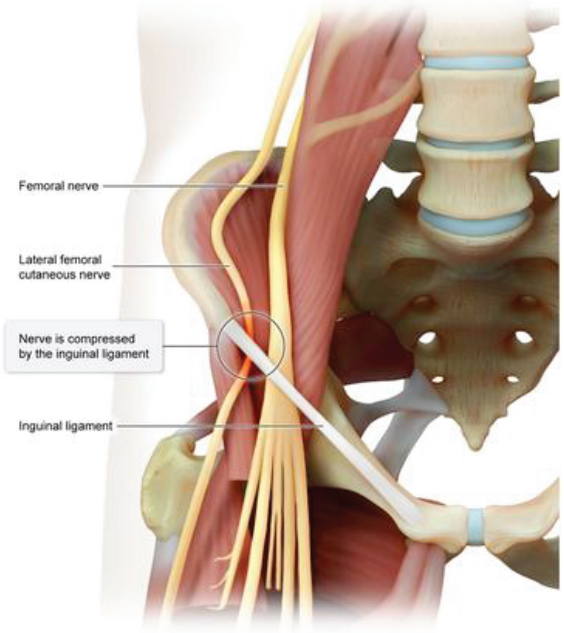
Lateral femoral cutaneous nerve & meralgia paresthetica

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This patient has pain and decreased sensation in the distribution of the lateral femoral cutaneous nerve (LFCN), consistent with **meralgia paresthetica** (MP). The LFCN is a branch of the lumbar plexus, originating from L2-L3. It runs lateral to the psoas muscle and exits the abdomen beneath the inguinal ligament. MP is a **compression mononeuropathy** of the LFCN at the inguinal ligament, typically caused by tight clothing (eg, belts) or by injury during surgery (eg, hip arthroplasty). Those with **obesity**, increased lumbar lordosis (eg, pregnancy), or **diabetes mellitus** are at increased risk.

MP presents with **pain, paresthesia, and numbness** in the **lateral thigh** above the knee. However, **strength is normal** because the LFCN does not contain motor fibers. The diagnosis is usually based on clinical findings. Most patients are managed with weight loss and avoidance of tight clothing.

**(Choice A)** The ilioinguinal nerve primarily provides sensory innervation to the upper medial thigh and genital region. It accompanies the spermatic cord through the superficial inguinal ring; injury during pelvic or hernia surgery can lead to chronic suprapubic or groin pain.

**(Choice C)** The obturator nerve is typically injured in anterior hip dislocation or pelvic surgery. Sensory symptoms occur in the medial thigh and are often associated with weakness in the adductor muscles.

**(Choice D)** The pelvic splanchnic nerves (S2-S4) provide parasympathetic innervation to the hindgut,



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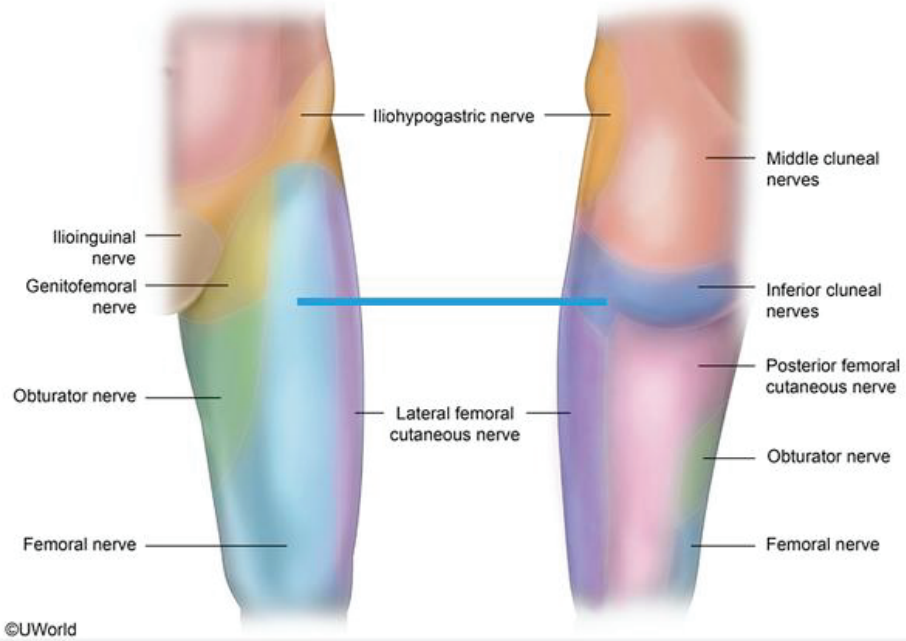
## Abdominopelvic cutaneous innervation

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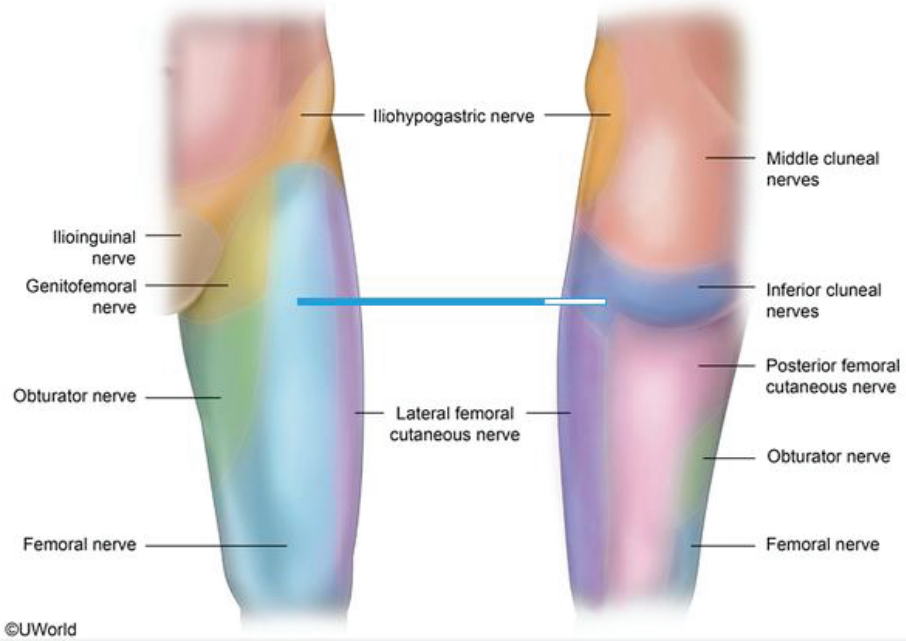
## Abdominopelvic cutaneous innervation

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## Obturator nerve

| Motor function | Cutaneous innervation |
|---|---|
| Adduction of the thigh | |



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symptoms occur in the medial thigh and are often associated with weakness in the adductor muscles.

**(Choice D)** The pelvic splanchnic nerves (S2-S4) provide parasympathetic innervation to the hindgut, bladder, and urinary sphincters and regulate peristalsis, bladder emptying, and defecation. They are commonly involved in cauda equina syndrome (eg, lumbar epidural metastasis) but are not vulnerable to external compression and would not cause lateral thigh symptoms.

**(Choice E)** The sciatic nerve arises from the L4-S3 nerve roots. Compression of the nerve (or contributing nerve roots) can occur at the spine (eg, herniated disc), piriformis muscle, greater sciatic foramen, or posterior thigh. Sciatica is a classic (though nonspecific) syndrome characterized by back and buttock pain that radiates down the posterior thigh to the foot; associated features include lower extremity weakness and a positive straight leg raise test.

**Educational objective:**
Meralgia paresthetica is caused by compression of the lateral femoral cutaneous nerve, typically due to tight clothing. It presents with pain, paresthesia, and numbness in the lateral thigh without motor weakness. Risk factors include obesity, pregnancy, and diabetes mellitus.

Anatomy Nervous System Meralgia paraesthetica



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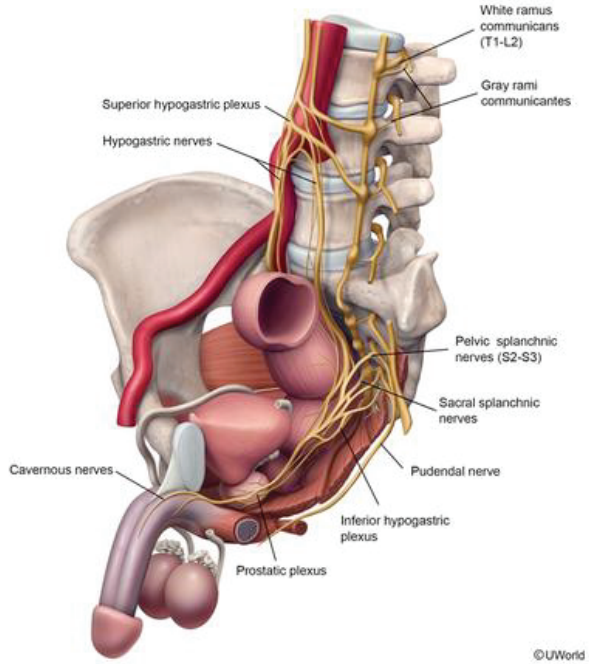
Exhibit Display

Pelvic autonomic nerves

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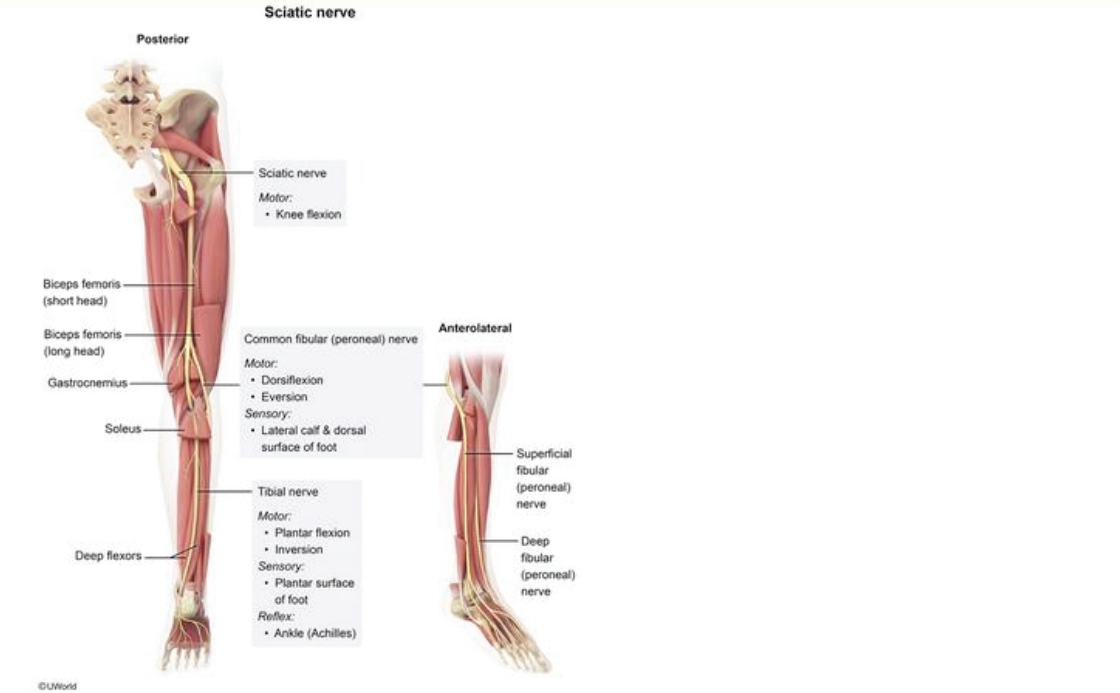


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A 54-year-old woman is evaluated in the clinic due to easy fatigability. The patient has had no weight gain or cold intolerance, and has no history of thyroid problems. Her medical history is significant for gastrectomy due to a nonhealing gastric ulcer. Physical examination shows a shiny tongue and pale palmar creases. Her gait is unstable when her eyes are closed, and vibration sense is markedly decreased over the lower extremities. There is mild symmetrical loss of strength affecting the proximal lower extremity muscles. Blood hemoglobin level is 7.2 g/dL and white blood cell count is 3,600/mm$^3$. Stool tests for occult blood are repeatedly negative. Which of the following spinal cord lesions is most likely present in this patient?

A.

B.

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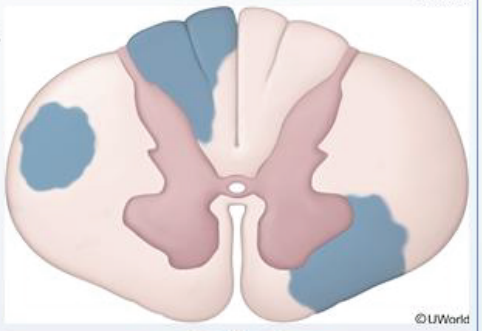
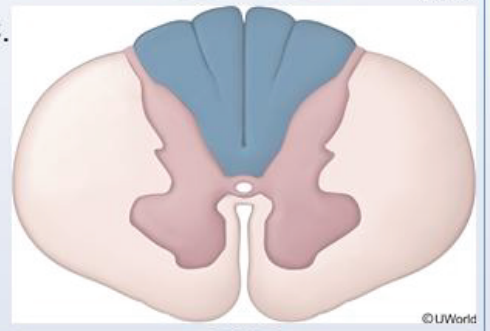
B.




C.




D.

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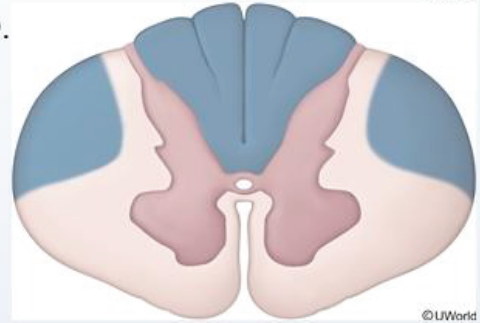
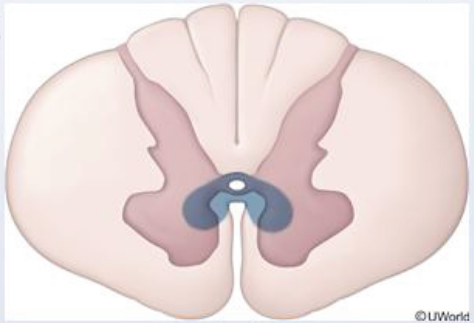



E.

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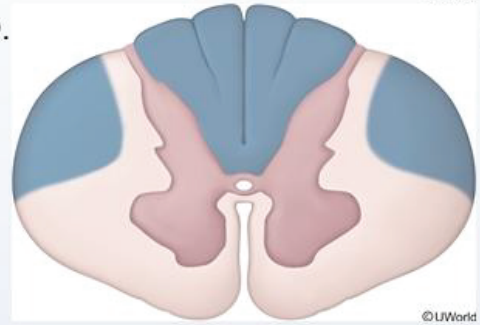
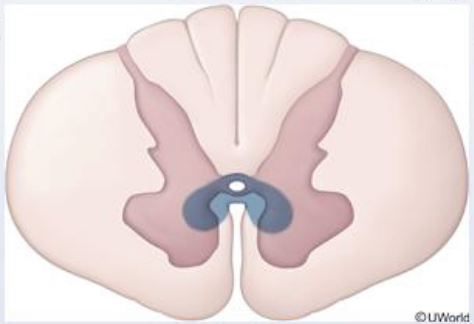



D. (70%)




E. (3%)




Incorrect
Correct answer

70%

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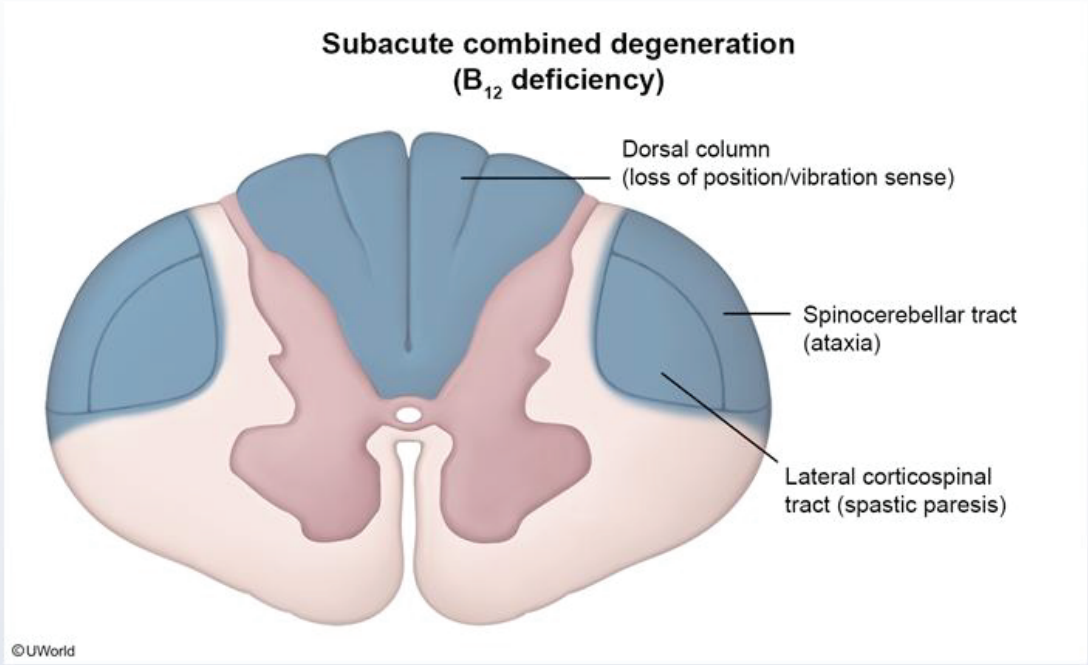


This patient is most likely suffering from **subacute combined degeneration** of the spinal cord, a condition that results from chronically low levels of vitamin $B_{12}$ (cobalamin). Low cobalamin levels may occur due to pernicious anemia (autoimmune gastritis with deficient intrinsic factor), **gastrectomy**, ileal resections,


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This patient is most likely suffering from **subacute combined degeneration** of the spinal cord, a condition that results from chronically low levels of vitamin $B_{12}$ (cobalamin). Low cobalamin levels may occur due to pernicious anemia (autoimmune gastritis with deficient intrinsic factor), **gastrectomy**, ileal resections, infection by the tapeworm *Diphyllobothrium latum*, and strict vegan diets containing no animal products for a prolonged period (4-5 years).

Anemia along with neurologic abnormalities is typical of **vitamin $B_{12}$ deficiency**. Vitamin $B_{12}$ is an important cofactor in DNA synthesis; therefore, hematologic manifestations of vitamin $B_{12}$ deficiency include megaloblastic anemia and pancytopenia. Elevated levels of methylmalonic acid also result in myelin synthesis abnormalities. Neurologic damage associated with vitamin $B_{12}$ deficiency classically includes subacute combined degeneration of the **dorsal columns** (loss of position and vibration sensation, sensory ataxia [positive Romberg sign]), **lateral corticospinal tracts** (spastic paresis), and spinocerebellar tracts (contributes to ataxia). Patients may also develop atrophic glossitis, which appears as a smooth, shiny, erythematous tongue.

**(Choice A)** Poliomyelitis and Werdnig-Hoffmann disease are associated with destruction of lower motor neurons in the anterior horn, which causes flaccid paralysis, muscle atrophy, and fasciculations.

**(Choice B)** Multiple sclerosis is an inflammatory demyelinating disorder affecting the white matter of the


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neurons in the anterior horn, which causes flaccid paralysis, muscle atrophy, and fasciculations.

**(Choice B)** Multiple sclerosis is an inflammatory demyelinating disorder affecting the white matter of the central nervous system in a random and asymmetric pattern. Patients typically present with neurologic deficits disseminated in space and time.

**(Choice C)** Tabes dorsalis (tertiary neurosyphilis) is characterized by degeneration of the dorsal root ganglia and dorsal columns. Although patients may have impaired vibratory sensation and proprioception, pancytopenia and atrophic glossitis are not characteristic. In addition, tabes dorsalis does not typically affect the lateral corticospinal tracts.

**(Choice E)** Syringomyelia is a central cavitation of the cervical spinal cord that is associated with damage to the anterior white commissure of the spinothalamic tract. Patients typically have bilateral loss of pain/temperature in the upper extremities. Expansion into the ventral horns may result in flaccid paralysis of the hand muscles.

**Educational objective:**

Neurologic damage associated with vitamin $B_{12}$ deficiency classically includes subacute combined degeneration of the dorsal columns (loss of position and vibration sensation, positive Romberg sign) and lateral corticospinal tracts (spastic paresis).



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**(Choice B)** Multiple sclerosis is an inflammatory demyelinating disorder affecting the white matter of the central nervous system in a random and asymmetric pattern. Patients typically present with neurologic deficits disseminated in space and time.

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Neurologic damage associated with vitamin $B_{12}$ deficiency classically includes subacute combined degeneration of the dorsal columns (loss of position and vibration sensation, positive Romberg sign) and lateral corticospinal tracts (spastic paresis).

**References**



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A 56-year-old man is evaluated in the clinic due to worsening lower extremity pain and weakness. The patient has had hematuria and intermittent burning on urination for the past year. He has no history of pelvic trauma or surgery. The patient has smoked a pack of cigarettes daily for the past 35 years. His urine culture is negative for bacterial growth. Urine cytology and cystoscopy confirm the diagnosis of transitional cell carcinoma. Abdominal CT shows an advanced bladder tumor compressing a nerve that passes through the obturator canal. Which of the following actions would most likely be impaired in this patient?

A. Abduction of the thigh
B. Adduction of the thigh
C. Extension of the leg
D. Extension of the thigh
E. Flexion of the thigh

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A 56-year-old man is evaluated in the clinic due to worsening lower extremity pain and weakness. The patient has had hematuria and intermittent burning on urination for the past year. He has no history of pelvic trauma or surgery. The patient has smoked a pack of cigarettes daily for the past 35 years. His urine culture is negative for bacterial growth. Urine cytology and cystoscopy confirm the diagnosis of transitional cell carcinoma. Abdominal CT shows an advanced bladder tumor compressing a nerve that passes through the obturator canal. Which of the following actions would most likely be impaired in this patient?

A. Abduction of the thigh (12%)
B. Adduction of the thigh (71%)
C. Extension of the leg (2%)
D. Extension of the thigh (7%)
E. Flexion of the thigh (6%)

71% 43 secs 09/26/2020



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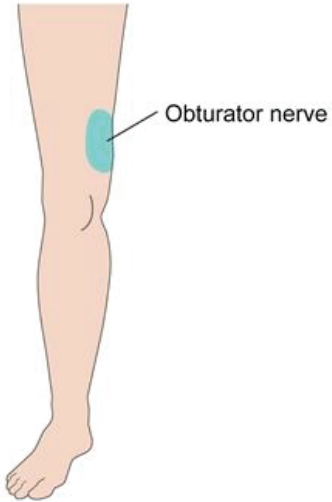
## Obturator nerve

| Nerve | Motor function | Cutaneous innervation |
|---|---|---|
| Obturator nerve | Adduction of the thigh | |

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The **obturator nerve** arises from the lumbar plexus and carries fibers from the L2-L4 spinal segments. It descends posteromedial to the iliopsoas muscle and courses along the lateral aspect of the lesser pelvis before descending through the **obturator canal**. The obturator nerve is the only major nerve that exits the pelvis through this canal. Once the nerve has entered the thigh, it supplies the obturator externus muscle and divides into anterior and posterior branches that supply the rest of the **thigh adductor** muscles (eg, adductor longus, brevis, magnus). The anterior division of the nerve gives off a terminal cutaneous branch that provides **sensation** over the **distal medial thigh**.

Obturator nerve injury is most commonly caused by compression due to pelvic trauma, surgery, or tumors (eg, bladder cancer). Patients typically present with weakness on thigh adduction and sensory loss in the distal medial thigh.

**(Choice A)** Abduction of the thigh is primarily accomplished by the gluteus medius, gluteus minimus, and tensor fascia lata, which are supplied by the superior gluteal nerve. This nerve exits the pelvis through the greater sciatic foramen above the piriformis.

**(Choice C)** Extension of the leg is mainly accomplished by the quadriceps femoris muscle group. These muscles are innervated by the femoral nerve, which gains access to the thigh deep to the midpoint of the



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greater sciatic foramen above the piriformis.

**(Choice C)** Extension of the leg is mainly accomplished by the quadriceps femoris muscle group. These muscles are innervated by the femoral nerve, which gains access to the thigh deep to the midpoint of the inguinal ligament.

**(Choice D)** Extension of the thigh is mostly accomplished by the gluteus maximus muscle, which is supplied by the inferior gluteal nerve. This nerve exits the pelvis through the greater sciatic foramen below the piriformis.

**(Choice E)** Flexion of the thigh is primarily accomplished by the psoas, iliacus, and sartorius muscles. The psoas is directly innervated by the lumbar plexus, and the iliacus is innervated by the femoral nerve.

**Educational objective:**

The obturator nerve is the only major nerve that exits the pelvis through the obturator foramen. Nerve injury typically results from compression (eg, due to pelvic trauma, surgery, or tumor) and presents with weakness on thigh adduction and sensory loss over the distal medial thigh.

**References**


- Obturator neuropathy.
- Obturator mononeuropathy caused by pelvic cancer: six cases.




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www.ncbi.nlm.nih.gov/pubmed/19468309

A 65-year-old man is brought to the emergency department due to acute mental status changes. The patient was having dinner with his family when he suddenly had difficulty using his fork and appeared confused. His medical problems include type 2 diabetes mellitus, hyperlipidemia, and hypertension. He is a school teacher and has a 40-pack-year smoking history. His blood pressure is 180/98 mm Hg and pulse is 98/min and regular. On physical examination, the patient is well oriented, answers questions appropriately, and has no motor, sensory, or visual deficits. Further evaluation shows that he has left-right disorientation and is unable to carry out simple calculations, read, or write. Noncontrast CT scan of the head reveals no acute intracranial hemorrhage. Which of the following brain areas is most likely affected in this patient?

A. Bilateral occipital lobes
B. Dominant parietal lobe
C. Dorsolateral medulla
D. Dorsolateral thalamus
E. Medial medulla


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patient was having dinner with his family when he suddenly had difficulty using his fork and appeared confused. His medical problems include type 2 diabetes mellitus, hyperlipidemia, and hypertension. He is a school teacher and has a 40-pack-year smoking history. His blood pressure is 180/98 mm Hg and pulse is 98/min and regular. On physical examination, the patient is well oriented, answers questions appropriately, and has no motor, sensory, or visual deficits. Further evaluation shows that he has left-right disorientation and is unable to carry out simple calculations, read, or write. Noncontrast CT scan of the head reveals no acute intracranial hemorrhage. Which of the following brain areas is most likely affected in this patient?

A. Bilateral occipital lobes
B. Dominant parietal lobe
C. Dorsolateral medulla
D. Dorsolateral thalamus
E. Medial medulla
F. Midbrain at level of superior colliculus


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a school teacher and has a 40-pack-year smoking history. His blood pressure is 180/98 mm Hg and pulse is 98/min and regular. On physical examination, the patient is well oriented, answers questions appropriately, and has no motor, sensory, or visual deficits. Further evaluation shows that he has left-right disorientation and is unable to carry out simple calculations, read, or write. Noncontrast CT scan of the head reveals no acute intracranial hemorrhage. Which of the following brain areas is most likely affected in this patient?

A. ~~Bilateral occipital lobes~~ (1%)
✓ B. Dominant parietal lobe (87%)
C. ~~Dorsolateral medulla~~ (1%)
D. ~~Dorsolateral thalamus~~ (5%)
E. Medial medulla (0%)
F. Midbrain at level of superior colliculus (3%)

Correct

87%
Answered correctly

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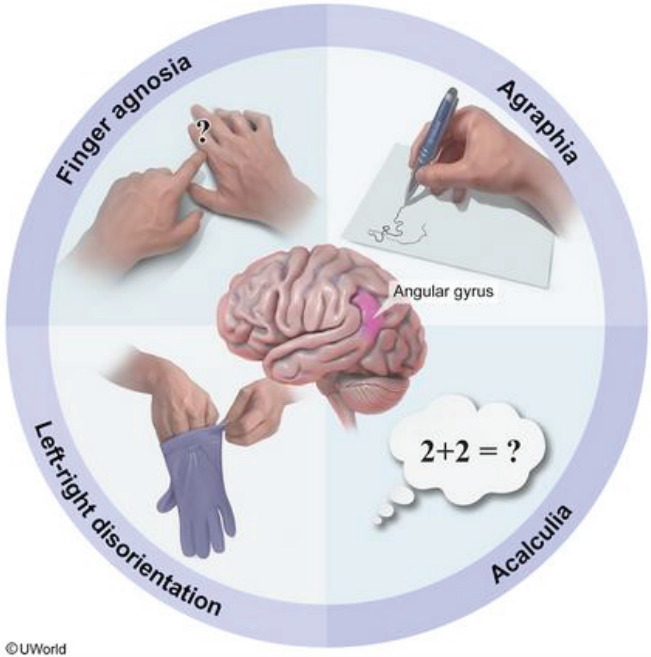
Gerstmann syndrome

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This patient's presentation is consistent with an acute ischemic stroke affecting the **angular gyrus** of the **dominant parietal lobe**, a brain region supplied by the middle cerebral artery. The angular gyrus is part of the parietal association cortex, an area that integrates multisensory (eg, visual, tactile, verbal) information to comprehend events and solve problems. Specifically, it is important for semantic processing, word reading and comprehension, and number processing. Damage to this area classically results in **Gerstmann syndrome**, a neurologic disorder characterized by a constellation of the following signs:

1. Agraphia (inability to write)
2. Acalculia (inability to carry out mathematical calculations)
3. Finger agnosia (inability to identify individual fingers on the hand)
4. Left-right disorientation

Although Gerstmann syndrome may occur as an isolated syndrome, lesions to the angular gyrus may also be associated with alexia (inability to read) and aphasia (impaired speech).

**(Choice A)** Damage to the bilateral occipital lobes can result in cortical blindness. Despite their obvious deficits, patients with this condition may confabulate and deny blindness.



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**(Choice A)** Damage to the bilateral occipital lobes can result in cortical blindness. Despite their obvious deficits, patients with this condition may confabulate and deny blindness.

**(Choice C)** Ischemic injury to the dorsolateral medulla, which is supplied by the posterior inferior cerebellar artery, can result in Wallenberg syndrome. Patients typically present with loss of pain/temperature over the ipsilateral face and contralateral body (due to damage of the spinal trigeminal and spinothalamic tracts), ipsilateral bulbar muscle weakness (nucleus ambiguus), vertigo (vestibular nuclei), ipsilateral limb ataxia (inferior cerebellar peduncle), and Horner syndrome (descending sympathetic fibers).

**(Choice D)** Acute strokes in the dorsolateral thalamus typically present with contralateral hemisensory loss. Weeks to months later, patients can develop excruciating pain on the side of their deficits (thalamic pain syndrome).

**(Choice E)** Medial medullary syndrome is an ischemic stroke syndrome caused by occlusion of the anterior spinal artery. Patients typically present with contralateral hemiparesis (due to damage of the lateral corticospinal tract), contralateral hemisensory loss (dorsal column medial lemniscal pathway), and ipsilateral tongue paralysis (hypoglossal nucleus).

**(Choice F)** Midbrain strokes at the level of the superior colliculus can result in upward gaze palsy, absent


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**(Choice D)** Acute strokes in the dorsolateral thalamus typically present with contralateral hemisensory loss. Weeks to months later, patients can develop excruciating pain on the side of their deficits (thalamic pain syndrome).

**(Choice E)** Medial medullary syndrome is an ischemic stroke syndrome caused by occlusion of the anterior spinal artery. Patients typically present with contralateral hemiparesis (due to damage of the lateral corticospinal tract), contralateral hemisensory loss (dorsal column medial lemniscal pathway), and ipsilateral tongue paralysis (hypoglossal nucleus).

**(Choice F)** Midbrain strokes at the level of the superior colliculus can result in upward gaze palsy, absent pupillary light reflex, and impaired convergence (Parinaud syndrome).

**Educational objective:**
Gerstmann syndrome results from damage to the angular gyrus of the dominant parietal lobe and is characterized by agraphia (inability to write), acalculia (inability to carry out mathematical calculations), finger agnosia (inability to identify individual fingers on the hand), and left-right disorientation.

**References**

- Gerstmann'S syndrome in acute stroke patients.


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A 22-year-old man is brought to the emergency department after a bar fight during which he received a knife wound to his neck. The patient is in moderate distress but is alert and can follow commands. Vital signs are stable. Neurologic examination shows right-sided hemiplegia. Loss of proprioception and vibratory sensation is present below the C8 dermatome on the right side. On the left side, there is loss of pain and temperature sensation below the T2 dermatome. MRI of this patient's spine will most likely reveal which of the following?

A. Complete transection of the spinal cord
B. Damage to the cervical dorsal roots on the right side
C. Lesion of the dorsal columns on the right side
D. Lesion of the medial longitudinal fasciculus on the right side
E. Right-sided hemisection of the spinal cord

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A 22-year-old man is brought to the emergency department after a bar fight during which he received a knife wound to his neck. The patient is in moderate distress but is alert and can follow commands. Vital signs are stable. Neurologic examination shows right-sided hemiplegia. Loss of proprioception and vibratory sensation is present below the C8 dermatome on the right side. On the left side, there is loss of pain and temperature sensation below the T2 dermatome. MRI of this patient's spine will most likely reveal which of the following?

A. ~~Complete transection of the spinal cord~~ (1%)

B. ~~Damage to the cervical dorsal roots on the right side~~ (2%)

C. Lesion of the dorsal columns on the right side (5%)

D. Lesion of the medial longitudinal fasciculus on the right side (2%)

✓ E. Right-sided hemisection of the spinal cord (88%)

Correct

88% Answered correctly

46 secs Time Spent

09/08/2020 Last Updated



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Explanation

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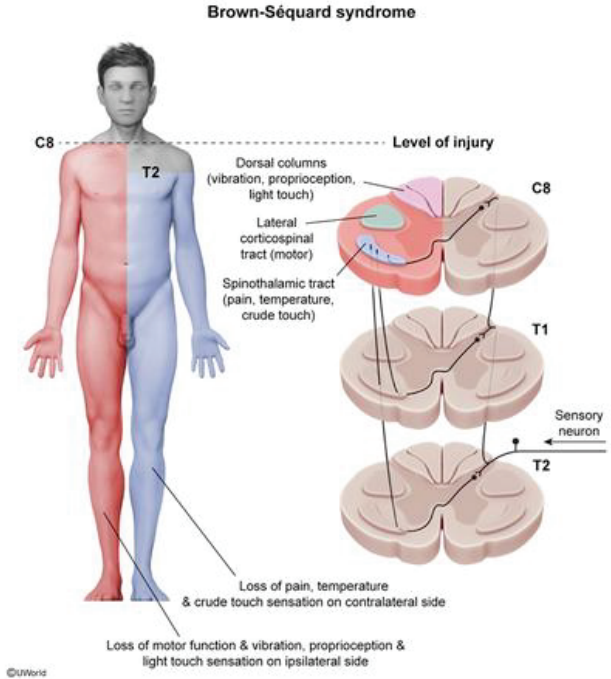


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This patient has a penetrating injury resulting in right-sided **hemisection** of the **spinal cord** at the C8 level. Spinal cord hemisection classically causes Brown-Séquard syndrome, which is characterized by the following tract lesions and clinical signs:

- **Anterior horn** (lower motor neuron) injury produces ipsilateral paralysis at the level of the lesion.
- Lateral **corticospinal tract** (upper motor neuron) injury results in ipsilateral paralysis below the level of the lesion.
- **Dorsal column** (gracile and cuneate fasciculi) involvement causes ipsilateral loss of vibration, proprioception, and light touch (ie, 2-point discrimination) sensation below the level of the lesion.
- **Spinothalamic tract** injury causes contralateral loss of pain and temperature (lateral spinothalamic) and crude touch (anterior spinothalamic) sensation 1-2 levels below the lesion.

Spinal cord injury above T1 can also cause ipsilateral Horner syndrome (ie, ptosis, miosis, anhidrosis) if there is concurrent damage to the oculosympathetic pathway.

**(Choice A)** Complete transection of the spinal cord would result in bilateral loss of all sensation and voluntary movement below the level of the lesion.

**(Choice B)** A lesion of the dorsal sensory roots would lead to ipsilateral loss of sensation and areflexia



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voluntary movement below the level of the lesion.

**(Choice B)** A lesion of the dorsal sensory roots would lead to ipsilateral loss of sensation and areflexia from the specific dermatome(s) affected.

**(Choice C)** A lesion of the dorsal columns on the right side would result only in ipsilateral loss of vibratory, proprioceptive, and light touch (ie, 2-point discrimination) sensation below the level of the lesion.

**(Choice D)** A lesion of the medial longitudinal fasciculus is associated with internuclear ophthalmoplegia, which is commonly seen in multiple sclerosis; it presents with impaired horizontal eye movement and weak adduction of the ipsilateral eye with simultaneous abduction nystagmus of the contralateral eye.

**Educational objective:**

Brown-Séquard syndrome results from hemisection of the spinal cord. It is characterized by ipsilateral paralysis due to corticospinal tract injury; ipsilateral loss of vibratory, proprioceptive, and light touch sensation (dorsal columns); and contralateral loss of pain, temperature, and crude touch sensation (spinothalamic tract) below the level of the injury.

**References**

- Brown-Sequard syndrome.


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A 20-year-old woman comes to the office due to blisters around her mouth associated with a mild burning sensation. She reports that she has been having frequent recurrence of these lesions, which resolve spontaneously within a few days. She has no medical problems and does not take any medications. Physical examination findings are shown in the image below.

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It is determined that the causative organism of this patient's condition remains in a latent state in the neuronal cell bodies of sensory ganglia. Upon reactivation, the virus is transported through the nerve axon to the skin. Which of the following proteins is most likely involved in the transport process leading to



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It is determined that the causative organism of this patient's condition remains in a latent state in the neuronal cell bodies of sensory ganglia. Upon reactivation, the virus is transported through the nerve axon to the skin. Which of the following proteins is most likely involved in the transport process leading to disease recurrence?

- A. Dynein
- B. Kinesin
- C. Lamin
- D. Selectin
- E. Spectrin
- F. Vimentin



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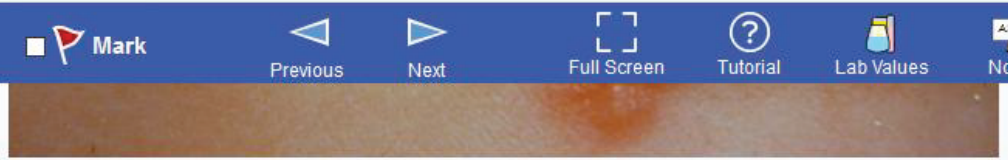

It is determined that the causative organism of this patient's condition remains in a latent state in the neuronal cell bodies of sensory ganglia. Upon reactivation, the virus is transported through the nerve axon to the skin. Which of the following proteins is most likely involved in the transport process leading to disease recurrence?

- A. Dynein (26%)
- ✓ B. Kinesin (65%)
- C. Lamin (1%)
- D. Selectin (1%)
- E. Spectrin (1%)
- F. Vimentin (3%)

Correct

65%
Answered correctly

20 secs
Time Spent

11/24/2020
Last Updated



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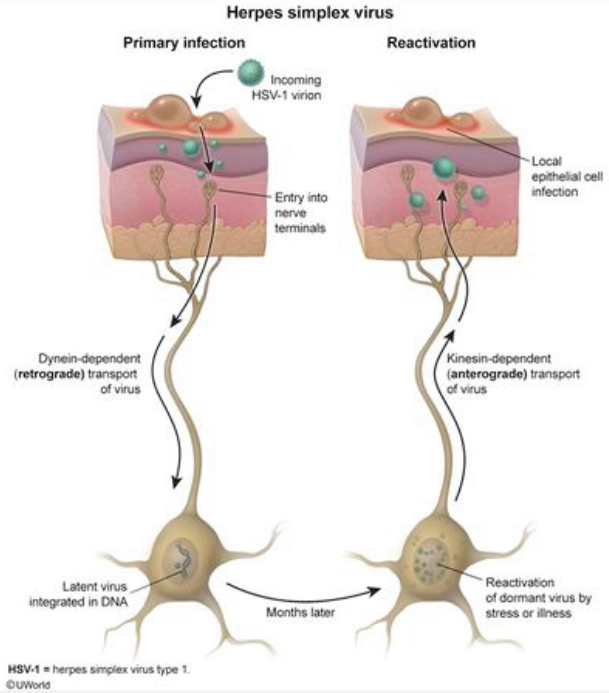


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HSV-1 = herpes simplex virus type 1.
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This patient is suffering from recurrent bouts of **herpes labialis** ("cold sores"), which is most commonly caused by ***herpes simplex virus 1* (*HSV-1*)**. Primary infection occurs following contact with an affected individual's saliva. Although it is often asymptomatic, infection can result in painful blister formation on the oral mucosa and surrounding skin of the mouth and lips. After resolution of the initial infection, the virus enters a latent phase where viral particles lay dormant in neural sensory ganglia (most commonly the trigeminal).

**Reactivation** of the virus occurs during times of stress or illness, resulting in recurrence of the characteristic perioral vesicular lesions. During reactivation, HSV particles rely on **anterograde axonal transport** to reach the skin and oral mucosa. Anterograde axonal transport is mediated by **kinesin**, a motor protein that moves intracellular cargo (eg, organelles, viral particles) away from the nucleus, down the axon, and toward the nerve terminal. Kinesin-mediated movement is powered by ATP hydrolysis and guided by microtubule filaments, which function as an intracellular "track" system.

**(Choice A)** Dynein is a microtubular motor protein that participates in retrograde axonal transport (ie, moving organelles toward the nucleus). Dynein is important in establishing the latent phase following primary HSV infection by transporting viral particles to the neural sensory ganglia. However, it is not


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**(Choice A)** Dynein is a microtubular motor protein that participates in retrograde axonal transport (ie, moving organelles toward the nucleus). Dynein is important in establishing the latent phase following primary HSV infection by transporting viral particles to the neural sensory ganglia. However, it is not responsible for disease recurrence.

**(Choice C)** Lamins are proteins that help form the fibrillar network that lines the inside of the nuclear envelope. In addition to providing structural support, they also help to organize the genome and regulate gene transcription.

**(Choice D)** Selectins are a group of cell adhesion molecules that are expressed on endothelial cells during the inflammatory response. They function to bind leukocytes, allowing them to exit blood vessels at the site of inflammation.

**(Choice E)** Spectrin is a cytoskeletal protein located intracellularly along the plasma membrane. It is responsible for maintaining the distinct shape of red blood cells. Protein defects may result in hereditary elliptocytosis and spherocytosis.

**(Choice F)** Vimentin is a type of intermediate filament expressed in mesenchymal cells. It is responsible for securing organelles inside the cytosol and provides resistance to mechanical stress.

**Educational objective:**



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gene transcription.

**(Choice D)** Selectins are a group of cell adhesion molecules that are expressed on endothelial cells during the inflammatory response. They function to bind leukocytes, allowing them to exit blood vessels at the site of inflammation.

**(Choice E)** Spectrin is a cytoskeletal protein located intracellularly along the plasma membrane. It is responsible for maintaining the distinct shape of red blood cells. Protein defects may result in hereditary elliptocytosis and spherocytosis.

**(Choice F)** Vimentin is a type of intermediate filament expressed in mesenchymal cells. It is responsible for securing organelles inside the cytosol and provides resistance to mechanical stress.

**Educational objective:**
Kinesin is a microtubule-associated motor protein that functions in the anterograde transport of materials and organelles within cells. Reactivation of latent herpes simplex virus requires anterograde transport of viral particles from neuronal cell bodies in the sensory ganglia to the skin and oral mucosa.

| Histology | Nervous System | Neuronal physiology |
|---|---|---|
| Subject | System | Topic |


https://t.me/USMLEWorldStep1

A 14-year-old, previously healthy girl is brought to the office due to recurrent headaches. The patient has had 4 episodes of severe, throbbing pain on the right side of her head over the last 2 months, with the most recent occurring a week ago. The headaches are often associated with nausea, and the patient has had occasional vomiting. Lying in a dark room and taking acetaminophen improve the pain. The episodes resolve after 4-5 hours. The patient has had no visual disturbances or focal weakness but has tingling and numbness on the right upper extremity prior to the headaches. Vital signs are within normal limits. Physical examination, including funduscopic and neurologic examination, shows no abnormalities. Which of the following is most likely involved in the pathogenesis of this patient's current condition?

A. Adrenal medullary catecholamines
B. Astrocyte epidermal growth factor receptors
C. Hypothalamic orexin A and B peptides
D. Thalamocortical fiber calcium channels
E. Trigeminal calcitonin gene-related peptides


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had 4 episodes of severe, throbbing pain on the right side of her head over the last 2 months, with the most recent occurring a week ago. The headaches are often associated with nausea, and the patient has had occasional vomiting. Lying in a dark room and taking acetaminophen improve the pain. The episodes resolve after 4-5 hours. The patient has had no visual disturbances or focal weakness but has tingling and numbness on the right upper extremity prior to the headaches. Vital signs are within normal limits. Physical examination, including funduscopic and neurologic examination, shows no abnormalities. Which of the following is most likely involved in the pathogenesis of this patient's current condition?

A. ~~Adrenal medullary catecholamines~~ (3%)

B. Astrocyte epidermal growth factor receptors (2%)

C. ~~Hypothalamic orexin A and B peptides~~ (6%)

D. Thalamocortical fiber calcium channels (14%)

E. Trigeminal calcitonin gene-related peptides (73%)

Incorrect
Correct answer

73%

02 mins, 26 secs

11/03/2020



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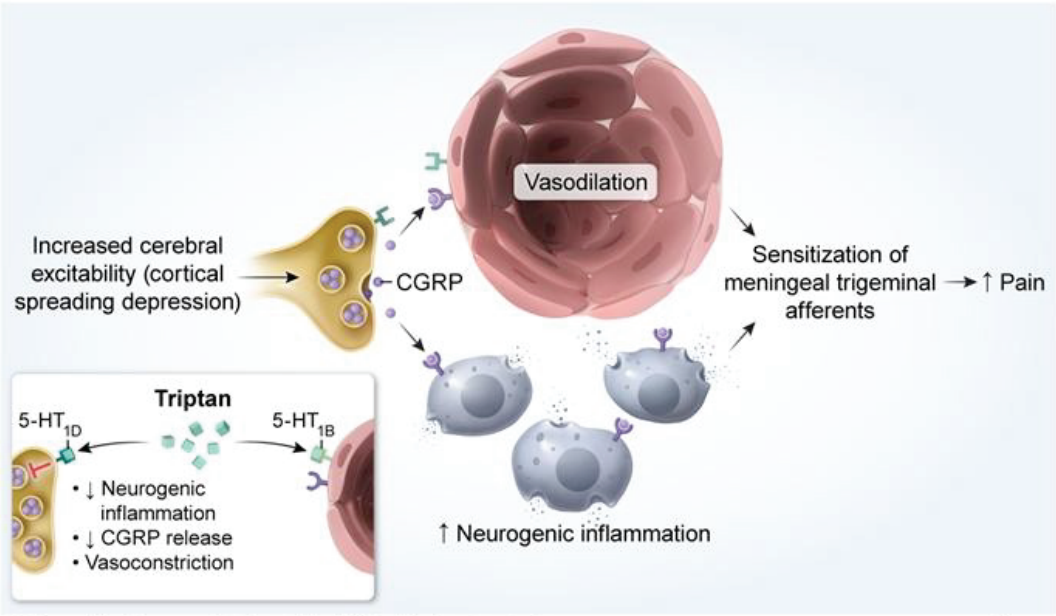
**Migraine pathogenesis & triptan mechanism of action**




**CGRP** = calcitonin gene-related peptide; **5-HT** = 5-hydroxytryptamine.

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This patient with a normal neurologic examination has episodic, throbbing, **unilateral headaches** associated with **nausea**, vomiting, and **light sensitivity**; findings characteristic of **migraines**. An **aura**



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**CGRP** = calcitonin gene-related peptide; **5-HT** = 5-hydroxytryptamine. ©UWorld

This patient with a normal neurologic examination has episodic, throbbing, **unilateral headaches** associated with **nausea**, vomiting, and **light sensitivity**; findings characteristic of **migraines**. An **aura** may precede the headache in some patients and is most commonly visual (eg, scotoma) or sensory (eg, unilateral extremity paresthesia).

The pathogenesis of migraines is multifactorial with a genetic predisposition to **increased cerebral excitability**, allowing a wave of **cortical spreading depression** to propagate across the cerebral cortex. Cortical spreading depression is likely involved in generating the pre-migraine **aura** and is associated with the abnormal activation of **trigeminal afferents**, which extend to the meninges and intracranial vasculature. This activation results in the release of **calcitonin gene-related peptide** (CGRP), a neuropeptide involved in **pain transmission**. CGRP also causes local vasodilation and increased neurogenic inflammation, which can further sensitize trigeminal afferents and increase pain.

The role of CGRP in migraine pathogenesis has been supported by the effectiveness of triptans ([5-$HT_{1B/1D}$] receptor agonists that decrease CGRP release) and anti-CGRP antibodies (eg, erenumab) in treating migraine headaches.

**(Choice A)** Pheochromocytoma is a catecholamine-producing adrenal medullary tumor that causes brief


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migraine headaches.

**(Choice A)** Pheochromocytoma is a catecholamine-producing adrenal medullary tumor that causes brief (<1 hr) episodic headaches associated with sweating, palpitations, and hypertension (rather than an aura).

**(Choice B)** Amplification of epidermal growth factor receptors is associated with the development of astrocytoma and glioblastoma. Headache and vomiting due to increased intracranial pressure are common but typically associated with other neurologic manifestations (eg, seizures, focal neurologic deficits).

**(Choice C)** Orexin A and B are excitatory neuropeptides that are produced in the lateral hypothalamus during wakefulness and inhibit the transition to REM sleep. Instead of episodic headaches, deficiency of these neuropeptides causes the daytime sleepiness, inappropriate bouts of REM sleep (ie, sleep attacks), and emotionally triggered transient muscle weakness (ie, cataplexy) seen in narcolepsy.

**(Choice D)** Dysfunction of the thalamocortical fiber calcium channels can contribute to the development of absence seizures, which are brief (10-20 sec) staring episodes with impairment of consciousness, not recurrent headaches.

**Educational objective:**
Migraines are episodic, unilateral, throbbing headaches associated with nausea, vomiting, and sensitivity to


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**(Choice B)** Amplification of epidermal growth factor receptors is associated with the development of astrocytoma and glioblastoma. Headache and vomiting due to increased intracranial pressure are common but typically associated with other neurologic manifestations (eg, seizures, focal neurologic deficits).

**(Choice C)** Orexin A and B are excitatory neuropeptides that are produced in the lateral hypothalamus during wakefulness and inhibit the transition to REM sleep. Instead of episodic headaches, deficiency of these neuropeptides causes the daytime sleepiness, inappropriate bouts of REM sleep (ie, sleep attacks), and emotionally triggered transient muscle weakness (ie, cataplexy) seen in narcolepsy.

**(Choice D)** Dysfunction of the thalamocortical fiber calcium channels can contribute to the development of absence seizures, which are brief (10-20 sec) staring episodes with impairment of consciousness, not recurrent headaches.

**Educational objective:**
Migraines are episodic, unilateral, throbbing headaches associated with nausea, vomiting, and sensitivity to light. The pathogenesis of migraines involves a genetic predisposition to increased cerebral excitability (eg, cortical spreading depression), which leads to abnormal neuronal activation of trigeminal afferents and the release of calcitonin gene-related peptide, a vasoactive neuropeptide involved in the transmission of pain signals.


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A 28-year-old man experiences worsening tinnitus and hearing loss. MRI of the brain reveals bilateral vestibular schwannomas. Genetic testing confirms a diagnosis of neurofibromatosis type 2. Additional imaging reveals a small meningioma at the C5 spinal level impinging upon the medial portion of the dorsal columns. Which of the following is the most likely earliest clinical manifestation of this lesion?

A. Decreased biceps tendon reflexes
B. Loss of crude touch sensation in the legs
C. Loss of pain sensation in the hands
D. Loss of position sensation in the fingers
E. Loss of vibration sensation in the toes

Submit



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A 28-year-old man experiences worsening tinnitus and hearing loss. MRI of the brain reveals bilateral vestibular schwannomas. Genetic testing confirms a diagnosis of neurofibromatosis type 2. Additional imaging reveals a small meningioma at the C5 spinal level impinging upon the medial portion of the dorsal columns. Which of the following is the most likely earliest clinical manifestation of this lesion?

- A. ~~Decreased biceps tendon reflexes~~ (12%)
- B. ~~Loss of crude touch sensation in the legs~~ (5%)
- C. ~~Loss of pain sensation in the hands~~ (6%)
- D. ~~Loss of position sensation in the fingers~~ (26%)
- ✓ E. Loss of vibration sensation in the toes (49%)

Correct

49%
Answered correctly

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Last Updated

Explanation



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This patient's lesion is affecting the **dorsal columns**, which convey **vibration and proprioception** sensation as well as **fine touch** (ie, 2-point discrimination). They are formed by incoming afferent axons of first-order neurons and are **arranged topographically** (ie, medial fibers from lower spinal levels, lateral fibers from higher spinal levels):

- **Gracile fasciculus**, located medially, which carries afferent information that enters the spinal cord **below T6** (lower half of the body) to the gracile nucleus in the medulla
- Cuneate fasciculus, located laterally, which carries afferent information that enters the spinal cord above T6 (upper half of the body) to the cuneate nucleus in the medulla

Therefore, this patient's **midline lesion** would affect the most medial fibers (gracile fasciculus) first, resulting in **loss of vibration sensation in the toes**.

**(Choice A)** A decreased biceps tendon reflex is more commonly associated with radiculopathy (C5 or C6) or other conditions affecting the lower motor neurons. This patient's posterior midline mass is most likely to affect the dorsal columns first before affecting the C5 motor neurons in the anterior horn.

**(Choices B and C)** Loss of crude touch sensation can occur with lesions involving the anterior spinothalamic tract; loss of pain sensation can occur with lesions of the lateral spinothalamic tract. These are located in the anterior portion of the spinal cord



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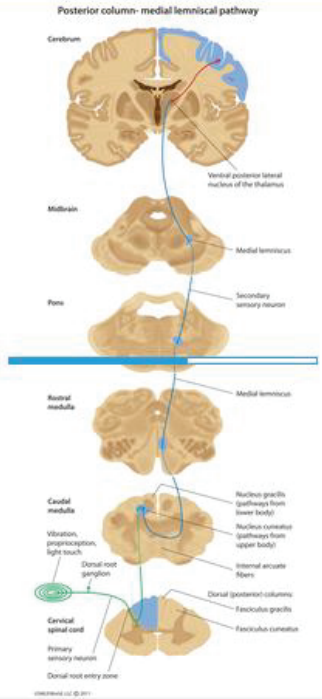


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are located in the anterior portion of the spinal cord



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affect the dorsal columns first before affecting the C5 motor neurons in the anterior horn.

**(Choices B and C)** Loss of crude touch sensation can occur with lesions involving the anterior spinothalamic tract; loss of pain sensation can occur with lesions of the lateral spinothalamic tract. These are located in the anterior portion of the spinal cord.

**(Choice D)** Loss of position sensation in the fingers could occur with a lesion affecting the lateral portion of the dorsal columns (ie, cuneate fasciculus). However, this patient's lesion is located medially and would compress the medial aspect first (eg, toe sensation).

**Educational objective:**

The dorsal columns are located in the posterior spinal cord and convey vibration, proprioception, and light touch sensation. Sensation from the lower limbs is carried in the gracile fasciculus, which is located in the medial aspect; sensation from the upper limbs is carried in the cuneate fasciculus, which is located in the lateral aspect.

| Anatomy | Nervous System | Peripheral neuropathy |
|---|---|---|
| Subject | System | Topic |

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A 6-month-old boy is brought to the office by his mother out of concern that he is not developing normally. He has been feeding regularly and has had no medical problems other than a mild respiratory infection a month earlier. However, the mother says, "he doesn't seem to be as interactive as my other children were at his age." Physical examination reveals delayed developmental milestones and hypotonia. Two years later, the child is found to have involuntary movements and demonstrates a tendency to aggressively bite his own lips and fingers. Laboratory analysis shows an elevated blood uric acid level. Activity of which of the following enzymes is most likely increased as a result of this patient's condition?

A. Aspartate carbamoyltransferase
B. Dihydroorotase
C. Hypoxanthine-guanine phosphoribosyltransferase
D. Phosphoribosyl pyrophosphate amidotransferase
E. Ribonucleotide reductase
F. Thymidylate synthase


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He has been feeding regularly and has had no medical problems other than a mild respiratory infection a month earlier. However, the mother says, "he doesn't seem to be as interactive as my other children were at his age." Physical examination reveals delayed developmental milestones and hypotonia. Two years later, the child is found to have involuntary movements and demonstrates a tendency to aggressively bite his own lips and fingers. Laboratory analysis shows an elevated blood uric acid level. Activity of which of the following enzymes is most likely increased as a result of this patient's condition?

A. ~~Aspartate carbamoyltransferase~~ (4%)
B. ~~Dihydroorotase~~ (3%)
C. Hypoxanthine-guanine phosphoribosyltransferase (43%)
D. Phosphoribosyl pyrophosphate amidotransferase (40%)
E. Ribonucleotide reductase (3%)
F. Thymidylate synthase (3%)

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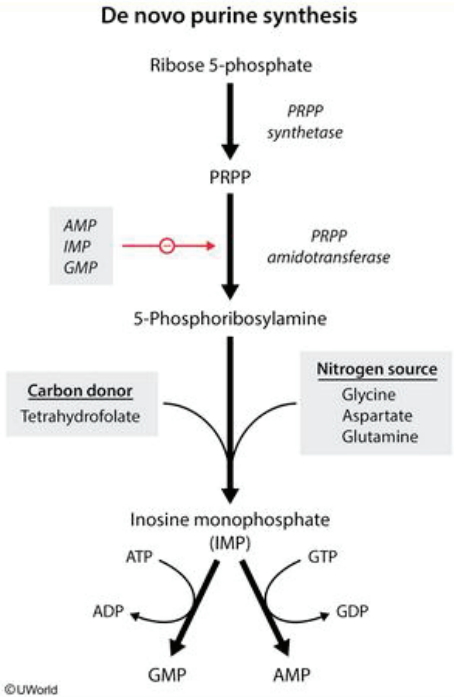


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This patient has **Lesch-Nyhan syndrome**, an X-linked recessive disorder characterized by the development of dystonia, choreoathetosis, **self-mutilation**, and **hyperuricemia** within the first few years of life. The condition is caused by deficiency of **hypoxanthine-guanine phosphoribosyltransferase** (HGPRT), an enzyme that normally functions in the purine salvage pathway to convert hypoxanthine back to inosine monophosphate and guanine back into guanosine monophosphate. The absence of HGPRT results in increased degradation of guanine and hypoxanthine bases into uric acid, which **increases** the demand for **de novo purine synthesis**.

The first step of purine synthesis is the formation of phosphoribosyl pyrophosphate (PRPP) by PRPP synthetase. PRPP can be used by adenine phosphoribosyltransferase and HGPRT for purine salvage, or it can be converted to phosphoribosylamine by PRPP amidotransferase in the first committed step of de novo purine synthesis. Because purine salvage is impaired in Lesch-Nyhan syndrome, the **activity of PRPP amidotransferase must increase** to supply a sufficient quantity of purine nucleotides.

**(Choices A, B, and F)** These enzymes are involved in pyrimidine synthesis. Their activity would not be significantly altered in Lesch-Nyhan syndrome, which impairs purine salvage.

**(Choice C)** The activity of HGPRT is decreased (not increased) in Lesch-Nyhan syndrome.



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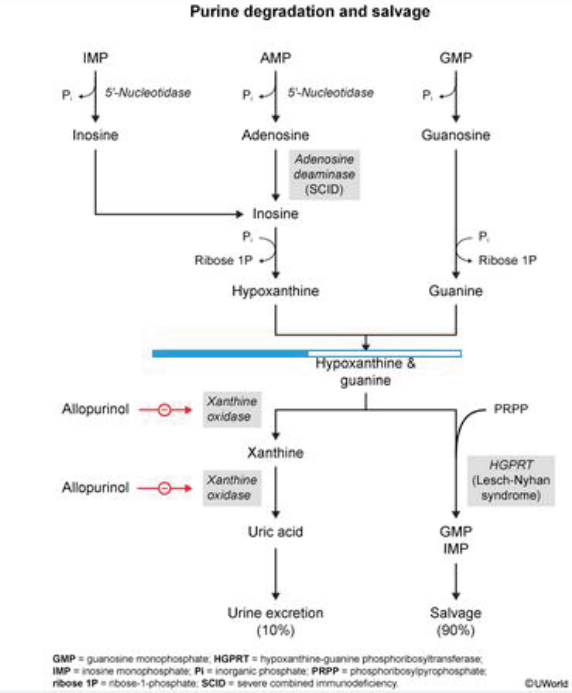


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(Choice C) The activity of HGPRT is decreased (not increased) in Lesch-Nyhan syndrome.



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**(Choices A, B, and F)** These enzymes are involved in pyrimidine synthesis. Their activity would not be significantly altered in Lesch-Nyhan syndrome, which impairs purine salvage.

**(Choice C)** The activity of HGPRT is decreased (not increased) in Lesch-Nyhan syndrome.

**(Choice E)** Purine and pyrimidine nucleotides are initially synthesized as bases attached to a ribose sugar. The enzyme ribonucleotide reductase converts ribose sugars to their deoxyribose forms for use in DNA synthesis. This enzyme is negatively regulated by accumulation of deoxyribose nucleotides; its activity is determined primarily by the cellular proliferation rate (increased cell division requires more deoxyribose nucleotides).

**Educational objective:**
Lesch-Nyhan syndrome is an X-linked recessive disorder caused by a defect in hypoxanthine-guanine phosphoribosyltransferase (HGPRT). This results in failure of the purine salvage pathway, leading to increased degradation of hypoxanthine and guanine to uric acid. De novo purine synthesis must increase to replace the lost bases, necessitating an increase in phosphoribosyl pyrophosphate (PRPP) amidotransferase activity.

| Biochemistry | Nervous System | Lesch Nyhan Syndrome |
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| Subject | System | Topic |


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A 12-year-old boy with mild intellectual disability is brought to the office by his adoptive parents for a routine physical examination. The parents say that the boy is adjusting well to a new school that has increased resources for children with learning disabilities. The patient was adopted as an infant and the birth family's history is unknown. His immunizations are up to date, and he has no allergies. Review of the patient's medical records is notable for cytogenetic studies that showed a small gap near the tip of the long arm of the X chromosome. Which of the following findings are likely to be present on this patient's physical examination?

A. Arachnodactyly, scoliosis, lens dislocation
B. Large ears, long face, macroorchidism
C. Short neck, low-set ears, epicanthic folds
D. Smooth philtrum, thin vermillion border
E. Tall stature, gynecomastia, infertility

Submit



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A 12-year-old boy with mild intellectual disability is brought to the office by his adoptive parents for a routine physical examination. The parents say that the boy is adjusting well to a new school that has increased resources for children with learning disabilities. The patient was adopted as an infant and the birth family's history is unknown. His immunizations are up to date, and he has no allergies. Review of the patient's medical records is notable for cytogenetic studies that showed a small gap near the tip of the long arm of the X chromosome. Which of the following findings are likely to be present on this patient's physical examination?

A. Arachnodactyly, scoliosis, lens dislocation (3%)
B. Large ears, long face, macroorchidism (83%)
C. Short neck, low-set ears, epicanthic folds (4%)
D. Smooth philtrum, thin vermillion border (3%)
E. Tall stature, gynecomastia, infertility (5%)


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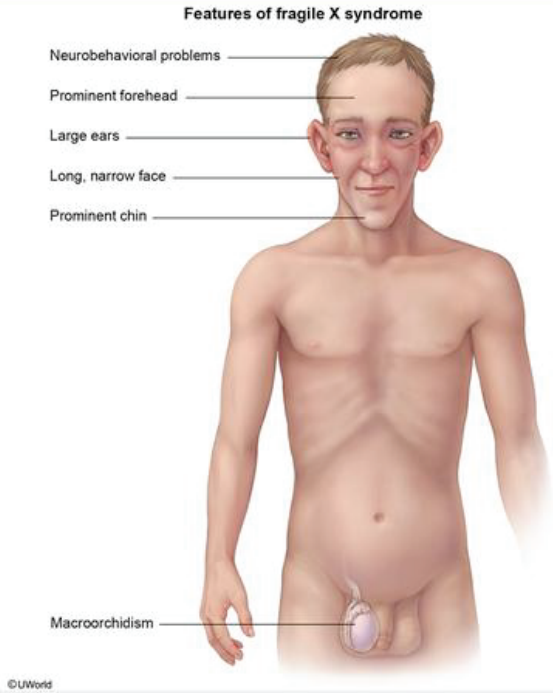


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Fragile X syndrome, an X-linked disorder, is the most common inherited cause of **intellectual disability**. The defect is an unstable **expansion of trinucleotide repeats** (**CGG**) in the fragile X mental retardation 1 (*FMR1*) gene, located on the long arm of the X chromosome. When the cells of affected individuals are cultured in folate-deficient medium, the area of increased repeats does not stain and appears "broken," hence the name "fragile X." Cytogenetic studies (chromosomal analysis) typically show a small gap near the tip of the long arm of the X chromosome.

The earliest manifestations of fragile X syndrome involve developmental delay, including delayed attainment of motor and language milestones. Mild to moderate intellectual disability is common. Classic physical features in fragile X syndrome include **macrocephaly**, a **long narrow face**, and a **prominent forehead**, **jaw**, **chin**, and **ears**. **Macroorchidism** (testicular enlargement) is also a key finding. All examination findings tend to be subtle during infancy and become most noticeable after puberty.

**(Choice A)** Cardinal features of Marfan syndrome are lens dislocation (ectopia lentis) and aortic root dilation. Other common abnormalities include arachnodactyly, scoliosis, and mitral valve prolapse. Cognition and chromosomal studies are typically normal in these patients.

**(Choice C)** Down syndrome is the most common genetic cause of intellectual disability. Classic findings include short neck, low-set ears, epicanthic folds, and slanted palpebral fissures. Cytogenetic studies


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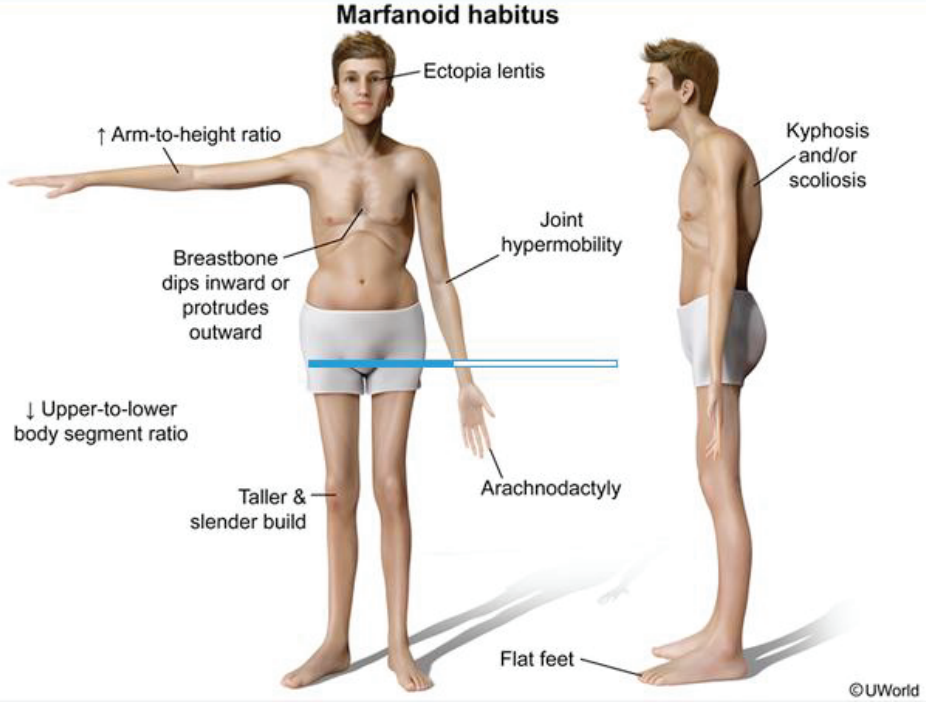


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Cognition and chromosomal studies are typically normal in these patients.

**(Choice C)** Down syndrome is the most common genetic cause of intellectual disability. Classic findings include short neck, low-set ears, epicanthic folds, and slanted palpebral fissures. Cytogenetic studies usually show a karyotype with 47 chromosomes, including 3 copies of chromosome 21.

**(Choice D)** Fetal alcohol syndrome is characterized by facial dysmorphisms (short palpebral fissures, indistinct philtrum, thin vermillion border), poor growth, and neurobehavioral problems.

**(Choice E)** Klinefelter syndrome (47,XXY) presents with tall stature, gynecomastia, and small, firm testes. Decreased testosterone secretion by fibrotic testes causes oligospermia and infertility.

**Educational objective:**

Fragile X syndrome, an X-linked disorder, is the most common cause of inherited intellectual disability. The pathogenesis involves an unstable expansion of trinucleotide repeats (CGG) in the fragile X mental retardation 1 (*FMR1*) gene. Key physical findings include dysmorphic facial features (eg, large jaw, protruding ears, long face) and macroorchidism.

**References**

- Fragile X syndrome: a review of associated medical problems.
- Health supervision for children with fragile X syndrome.



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Cognition and chromosomal studies are typically normal in these patients.

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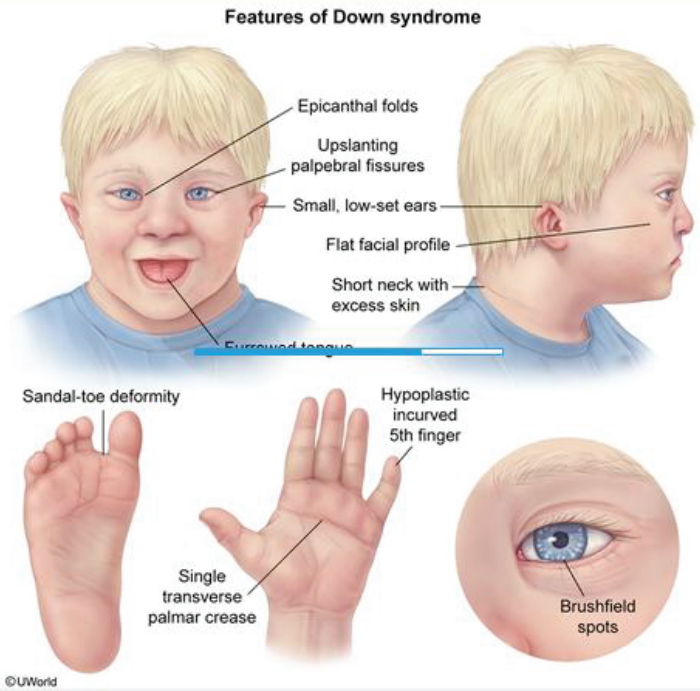


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Health supervision for children with fragile X syndrome.



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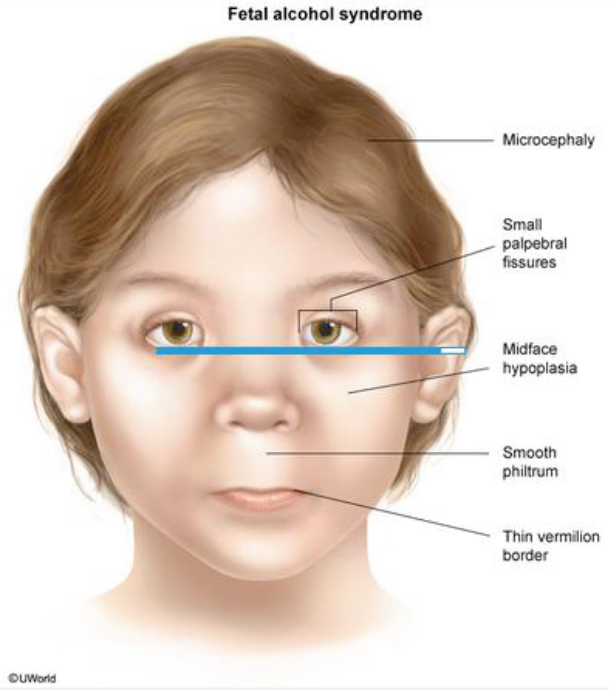


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Cognition and chromosomal studies are typically normal in these patients.

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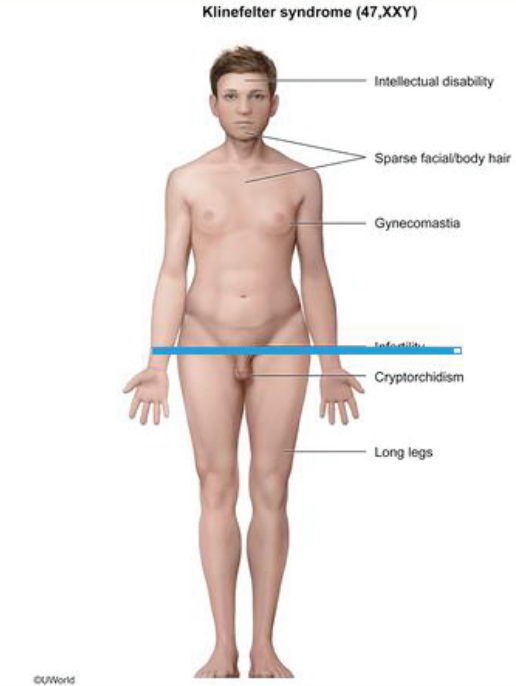


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Health supervision for children with fragile X syndrome.



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A 2-month-old boy is brought to the clinic for irritability, poor feeding, and frequent vomiting. Weight is at the 15th percentile, and head circumference is at the 96th percentile. Lung sounds are clear throughout, and heart auscultation reveals no murmurs. The abdomen is soft and nondistended. There is hepatosplenomegaly. Diffusely reduced muscle tone is present in all extremities. Funduscopy reveals white-yellow chorioretinal lesions in both eyes. MRI of the brain shows enlarged ventricles and scattered intracranial calcifications. Which of the following is the most likely cause of this patient's condition?

A. Chromosomal abnormality
B. Intrapartum infection
C. In utero infection
D. Postpartum infection
E. Single gene defect

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A. Chromosomal abnormality (2%)
B. ~~Intrapartum infection~~ (16%)
C. In utero infection (71%)
D. ~~Postpartum infection~~ (3%)
E. Single gene defect (5%)

Correct

71%
Answered correctly

01 min, 29 secs
Time Spent

12/14/2020
Last Updated



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| Key features of congenital infections* | |
|---|---|
| **Toxoplasmosis** | • Chorioretinitis<br>• Hydrocephalus<br>• Diffuse intracranial calcifications |
| **Syphilis** | • Rhinorrhea<br>• Skeletal anomalies<br>• Desquamating rash (palms/soles) |
| **Rubella** | • Cataracts<br>• Heart defects (eg, PDA)<br>• Sensorineural hearing loss |
| **Cytomegalovirus** | • Periventricular calcifications<br>• Microcephaly<br>• Sensorineural hearing loss |
| **Herpes simplex virus** | • Vesicular/ulcerative rash |

*Nonspecific findings include growth restriction, jaundice, hepatosplenomegaly & blueberry muffin



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*Nonspecific findings include growth restriction, jaundice, hepatosplenomegaly & blueberry muffin rash.

**PDA** = patent ductus arteriosus.

This patient with hydrocephalus, intracranial calcifications, and chorioretinitis has the classic triad of findings for **congenital toxoplasmosis**. Congenital infections (eg, **TORCH infections** [**T**oxoplasmosis, **O**ther infections, **R**ubella, **C**ytomegalovirus, and **H**erpes simplex]) are acquired **in utero** due to **transplacental transmission** from an infected mother. Maternal infection may be asymptomatic or mild but can severely affect the fetus, particularly when contracted early in pregnancy.

**Prolonged inflammation** of the CNS during fetal development can lead to chronic inflammatory findings such as **intracranial calcifications**. Obstructive **hydrocephalus** can also occur, as seen in this patient with ventriculomegaly, enlarged head circumference, and signs of increased intracranial pressure (eg, vomiting, hypotonia). Chronic chorioretinal inflammation (ie, **chorioretinitis**) produces white-yellow **retinal scars** that are visible on funduscopy.

Other nonspecific findings that may raise suspicion for in utero infection include growth restriction, hepatosplenomegaly (due to fetal reticuloendothelial activation), and rash.

**(Choices A and E)** Although chromosomal abnormalities and single gene defects can lead to congenital


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**(Choices A and E)** Although chromosomal abnormalities and single gene defects can lead to congenital disorders associated with neurologic abnormalities, chorioretinitis is highly associated with infection, particularly when presenting with the classic triad of features for toxoplasmosis.

**(Choice B)** Intrapartum transmission of certain bacteria (eg, group B *Streptococcus*) or viruses (eg, herpes simplex virus) can cause meningitis or encephalitis beyond the neonatal period, and presentation can include irritability, poor feeding, vomiting, and hypotonia. However, fever would be expected, and chorioretinal lesions would not be seen.

**(Choice D)** Postpartum infection with pathogens such as *Toxoplasma* and cytomegalovirus is often asymptomatic or can cause mild, self-limited fever, rash, and lymphadenopathy. Late findings of prolonged infection and inflammation (eg, intracranial calcifications, chorioretinitis) typically occur only with intrauterine infection.

**Educational objective:**
Congenital toxoplasmosis is an infection acquired in utero that can present with hydrocephalus, intracranial calcifications, and chorioretinitis due to prolonged CNS inflammation.

| Microbiology | Nervous System | Toxoplasmosis |
|---|---|---|
| Subject | System | Topic |



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A 69-year-old hospitalized woman is evaluated for new-onset weakness of the right foot. The patient has a history of chronic hip pain due to osteoarthritis and underwent left total hip arthroplasty under general anesthesia while in the right lateral decubitus position 2 days ago. Since the surgery, she has had difficulty moving her right foot. Other medical conditions include lumbar spinal stenosis, hypertension, type 2 diabetes mellitus, and a small ischemic stroke with no residual deficit. On examination of the right lower extremity, the patient is unable to dorsiflex or evert the foot or extend the toes. Sensation is decreased over the dorsum of the right foot. The rest of the neurologic examination of the right lower extremity is normal. Injury to which of the following structures is the most likely cause of this patient's current symptoms?

A. Common fibular nerve
B. Deep fibular nerve
C. Femoral nerve
D. Lateral sural cutaneous nerve
E. Lumbosacral spinal nerve roots


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moving her right foot. Other medical conditions include lumbar spinal stenosis, hypertension, type 2 diabetes mellitus, and a small ischemic stroke with no residual deficit. On examination of the right lower extremity, the patient is unable to dorsiflex or evert the foot or extend the toes. Sensation is decreased over the dorsum of the right foot. The rest of the neurologic examination of the right lower extremity is normal. Injury to which of the following structures is the most likely cause of this patient's current symptoms?

- A. Common fibular nerve
- B. Deep fibular nerve
- C. Femoral nerve
- D. Lateral sural cutaneous nerve
- E. Lumbosacral spinal nerve roots
- F. Sciatic nerve
- G. Tibial nerve

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moving her right foot. Other medical conditions include lumbar spinal stenosis, hypertension, type 2 diabetes mellitus, and a small ischemic stroke with no residual deficit. On examination of the right lower extremity, the patient is unable to dorsiflex or evert the foot or extend the toes. Sensation is decreased over the dorsum of the right foot. The rest of the neurologic examination of the right lower extremity is normal. Injury to which of the following structures is the most likely cause of this patient's current symptoms?

- A. Common fibular nerve (70%) ✓
- B. Deep fibular nerve (13%)
- C. Femoral nerve (1%)
- D. ~~Lateral sural cutaneous nerve~~ (1%)
- E. Lumbosacral spinal nerve roots (1%)
- F. Sciatic nerve (3%)
- G. Tibial nerve (7%)


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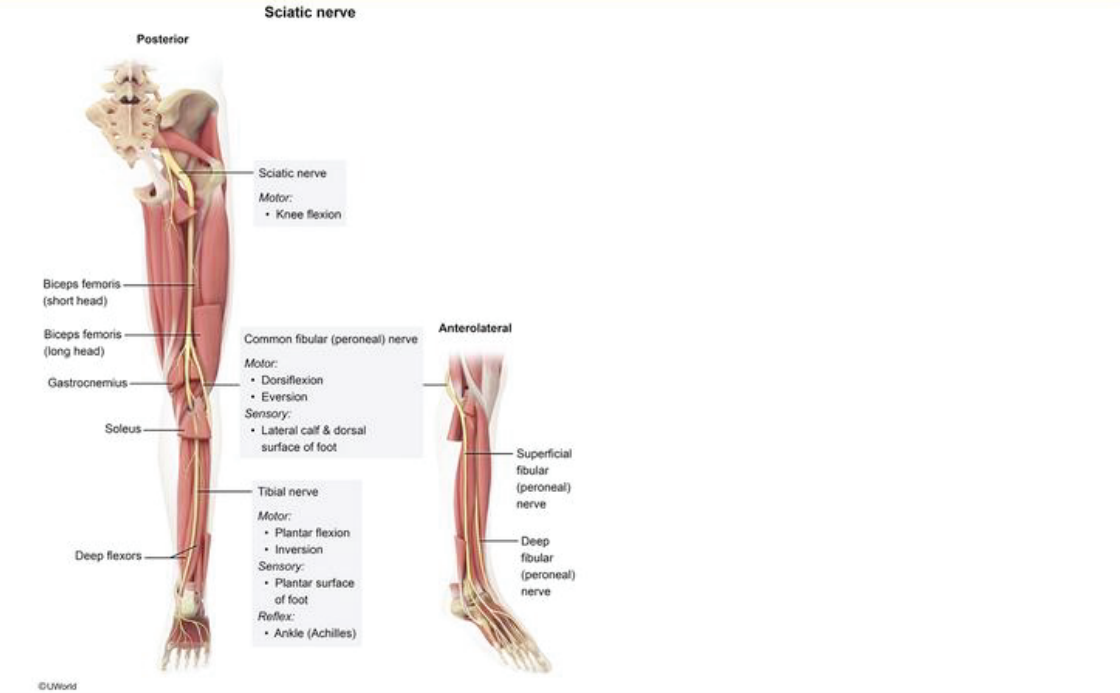


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Gastrocnemius
• Dorsiflexion



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The **common fibular** (peroneal) nerve originates in the popliteal fossa as the lateral branch of the sciatic nerve. From there, it courses laterally around the head and neck of the fibula before dividing into the deep and superficial fibular nerves. Because of its proximity to the **lateral neck** of the **fibula**, the common fibular nerve is particularly susceptible to **compression** from a leg cast or during prolonged time in the lateral decubitus position (eg, during surgical procedures).

Common fibular neuropathy characteristically presents with deficits involving both the deep fibular (eg, weakness in foot dorsiflexion and toe extension) and the superficial fibular (eg, weakness in foot eversion, sensory loss over the dorsal foot) nerves **(Choice B)**. In an ambulatory patient, gait examination typically shows **foot drop** due to loss of dorsiflexion, with the affected foot lifted high off the ground to compensate (ie, steppage gait).

**(Choice C)** Although the femoral nerve is rarely injured during hip replacement, this injury would result in weakness on hip flexion and knee extension along with loss of sensation over the anterior thigh.

**(Choice D)** The lateral sural cutaneous nerve is a branch of the common fibular nerve that provides sensory innervation to the posterolateral leg; it does not provide motor innervation.

**(Choice E)** Irritation of the lumbosacral spinal nerve roots can cause variable sensorimotor deficits due to



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sensory innervation to the posterolateral leg; it does not provide motor innervation.

**(Choice E)** Irritation of the lumbosacral spinal nerve roots can cause variable sensorimotor deficits due to the involvement of multiple myotomes and dermatomes. This patient's sensorimotor findings are specific for common fibular nerve injury.

**(Choice F)** The most common cause of proximal sciatic nerve injury is trauma or surgery involving the hip joint. However, sciatic nerve injury causes deficits in the fibular, tibial, and sural nerve distributions, with loss of sensation over the posterior leg and weakness involving the hamstrings and most of the muscles of the lower leg.

**(Choice G)** The tibial nerve can be injured at the knee by trauma or compression (eg, Baker cyst in the popliteal fossa). Proximal tibial neuropathy usually causes weakness in foot plantar flexion and decreased sensation over the sole of the foot.

**Educational objective:**

The common fibular nerve is susceptible to injury at the lateral neck of the fibula due to compression (ie, prolonged lying on the affected side) or fracture. Patients typically have weakness in foot dorsiflexion, foot eversion, and toe extension along with sensory loss over the lateral leg and dorsal foot.



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(Choice D) The lateral sural cutaneous nerve is a branch of the common fibular nerve that provides

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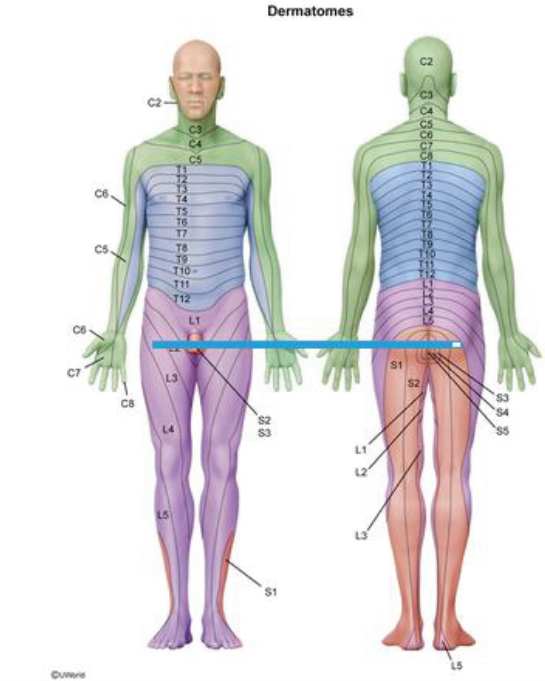


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A 64-year-old woman with history of lung cancer comes to the office due to persistent chest pain. The patient has squamous cell carcinoma of the right upper lobe that has invaded the pleura and the 4th and 5th ribs. She has had severe right sided chest pain that is exacerbated by movement or cough. The patient was given an opioid analgesic but could not take them at the prescribed dose due to excessive sedation. Physical examination shows tenderness to palpation of the right chest wall. A nerve block procedure is planned to control the pain by injecting a local anesthetic agent in the vicinity of the involved neural structure. Which of the following is the most appropriate treatment target?

A. Inferior cervical ganglion
B. Intercostal nerves
C. Phrenic nerve
D. Pulmonary plexus
E. Thoracic sympathetic trunk

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A. ~~Inferior cervical ganglion~~ (4%)
B. Intercostal nerves (77%)
C. ~~Phrenic nerve~~ (10%)
D. ~~Pulmonary plexus~~ (2%)
E. Thoracic sympathetic trunk (5%)

77% 02 mins, 09 secs 11/30/2020


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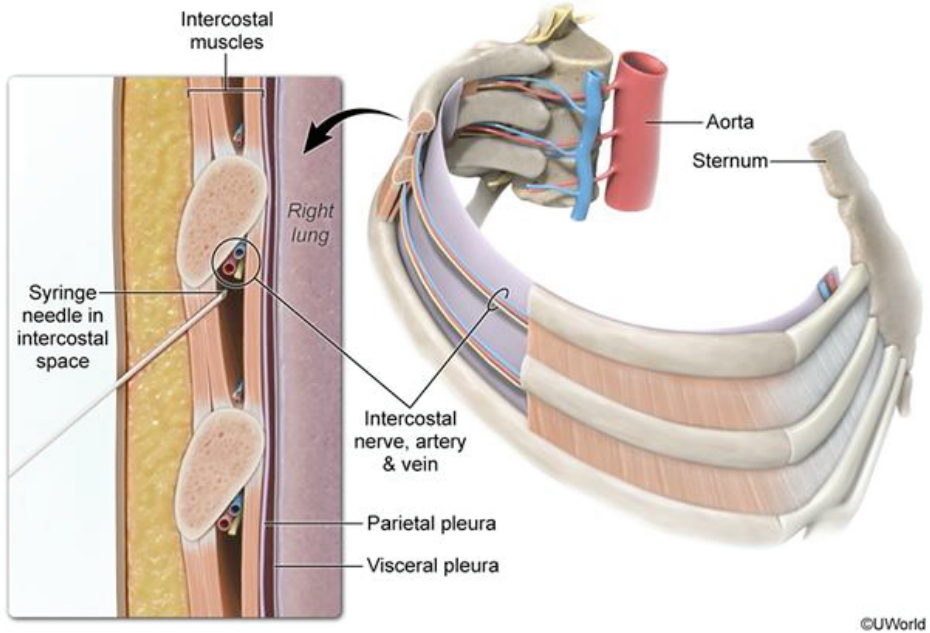
## Intercostal nerve block

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This patient has severe **chest wall pain** due to cancer invading the **parietal pleura and ribs**. She is unable to take opioid medication due to intolerable adverse effects, so she should be offered other interventional pain management strategies. Options include nerve blocks (eg, injection of anesthetic near the nerve), neurolysis (eg, physical or chemical nerve destruction), and neuromodulation (eg, spinal cord stimulation).

This patient is undergoing an **intercostal nerve block** to improve her pain control. Sensation from the parietal pleura, ribs, and overlying skin is mediated by thoracic intercostal nerves that derive from the ventral rami of the thoracic spinal nerves. An intercostal nerve block provides anesthesia over the dermatomal distribution of the nerve that is anesthetized. The intercostal vein, artery, and nerve lie in the **subcostal groove** along the lower border of the rib and therefore provide a straightforward target for a nerve block.

**(Choices A and E)** The inferior cervical ganglion and the thoracic sympathetic trunk are part of the sympathetic nervous system. They help convey thoracic and upper abdominal visceral pain but do not carry somatic sensory information. Nerve blockade here would decrease sympathetic activity (eg, decrease sweating in hyperhidrosis) but would not significantly improve chest wall pain.



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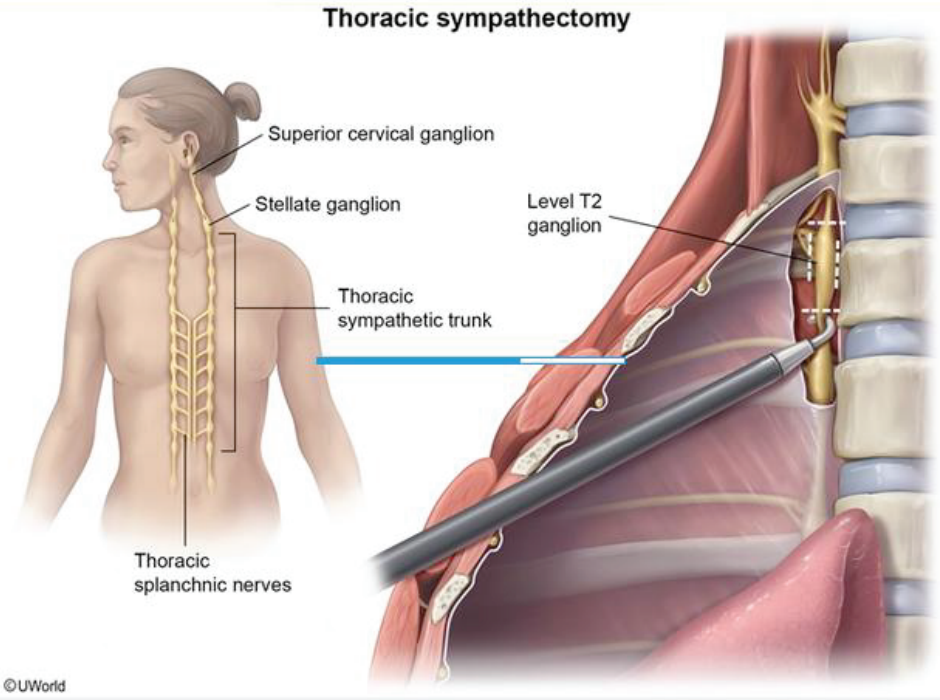


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decrease sweating in hyperhidrosis) but would not significantly improve chest wall pain.

**(Choice C)** The phrenic nerve, which is derived from the C3-C5 nerve roots, delivers motor innervation to the diaphragm and carries pain fibers from the diaphragmatic and mediastinal pleura (not the costal pleura). Pain due to diaphragmatic and mediastinal pleura is often referred to the C3-C5 distribution at the base of the neck and over the shoulder. In addition, a nerve block that could paralyze the diaphragm is not typically recommended.

**(Choice D)** The pulmonary plexus is derived from branches of the vagus nerve and the sympathetic trunk. It innervates the visceral pleura but not the parietal pleura or the chest wall. Unlike the parietal pleura, the visceral pleura can only detect stretch and is not sensitive to pain.

**Educational objective:**
Sensation to the parietal pleura, chest wall, and skin of the chest is supplied by the intercostal nerves that derive from the ventral nerve rami. A nerve block can be used to control pain from these areas when opioids are ineffective, contraindicated, or have intolerable adverse effects.

| Anatomy | Nervous System | Lung cancer |
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| Subject | System | Topic |

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decrease sweating in hyperhidrosis) but would not significantly improve chest wall pain.

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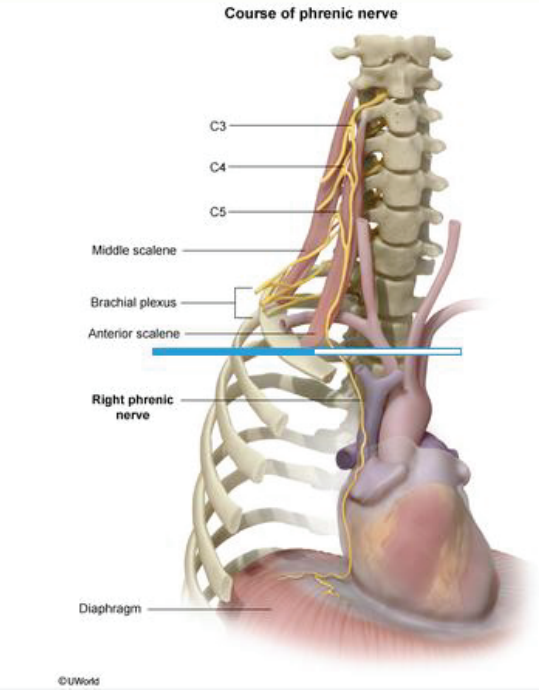


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A 27-year-old woman, gravida 1 para 0, at 37 weeks gestation comes to the emergency department after spontaneous rupture of membranes with leakage of blood mixed with fluid. Emergency cesarean delivery is performed due to severe fetal bradycardia. On delivery, the neonate is apneic and hypotonic. Resuscitation with endotracheal intubation and assisted ventilation is performed, which improves bradycardia. Apgar scores are <5 at 5 and 10 minutes. Umbilical cord blood analysis shows high anion gap metabolic acidosis. Controlled hypothermia to maintain body temperature at 33-35 C (91.4-95 F) is begun. This therapy is most likely to provide benefit via which of the following mechanisms?

A. Decreased activation of the coagulation cascade

B. Decreased reactive oxygen species–mediated neuronal injury

C. Increased conversion of bilirubin to less toxic water-soluble isomers

D. Increased hepatic clearance of lactic acid

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A. ~~Decreased activation of the coagulation cascade~~ (8%)

✓ B. Decreased reactive oxygen species–mediated neuronal injury (63%)

C. ~~Increased conversion of bilirubin to less toxic water-soluble isomers~~ (2%)

D. Increased hepatic clearance of lactic acid (25%)

Correct

63%
Answered correctly

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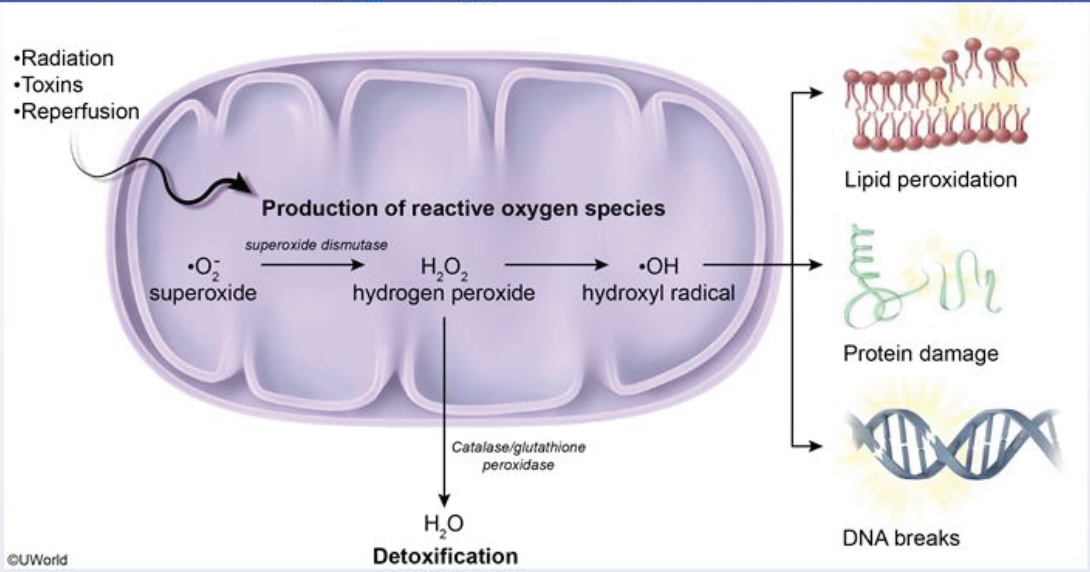


This early-term infant has sustained **hypoxic-ischemic injury** during delivery and is at risk of worsening neonatal encephalopathy (eg, decreased consciousness, impaired respiration, seizures). Hypoxia can lead to neuronal injury through multiple injury cascades, many of which lead to the **formation of reactive oxygen species** (ROS). ROS can mediate cellular damage of DNA, cell membranes, proteins, and enzymes, leading to widespread neuronal death.


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**Therapeutic hypothermia** (maintenance of temperature at 33-35 C [91.4-95 F]) leads to improved neurologic outcomes in a variety of hypoxia-induced injuries (eg, after cardiac arrest, seizures). The formation of ROS after ischemic injury is temperature dependent, so it can be decreased by therapeutic hypothermia. In addition, therapeutic hypothermia decreases cerebral blood flow, oxygen consumption, and glucose metabolism, thereby **decreasing the formation of ROS** due to both cellular metabolism and reperfusion.

Therapeutic hypothermia has other beneficial effects, including lowering intracranial pressure, reducing excitatory neurotransmitters, and decreasing activation of inflammatory and apoptotic pathways (eg, blocks tumor necrosis factor and caspase pathways).

**(Choice A)** Therapeutic hypothermia impairs both platelets and clotting factors, which, rather than being neuroprotective, can lead to an increased risk of bleeding complications (eg, intracranial hemorrhage).

**(Choice C)** In neonates with severe hyperbilirubinemia, unbound, lipid-soluble bilirubin can cross the blood-brain barrier. This neurotoxic bilirubin preferentially deposits in the basal ganglia and brainstem nuclei, leading to permanent neurologic damage. The primary treatment for hyperbilirubinemia converts bilirubin to a *more water-soluble form (isomers)* that can be excreted. However, this is accomplished through *phototherapy* rather than therapeutic hypothermia.


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nuclei, leading to permanent neurologic damage. The primary treatment for hyperbilirubinemia converts bilirubin to a *more water-soluble form (isomers)* that can be excreted. However, this is accomplished through *phototherapy* rather than therapeutic hypothermia.

**(Choice D)** This patient has anion gap metabolic acidosis due to lactic acidosis caused by tissue hypoxia. Although the liver is responsible primarily for clearing lactate, its rate of clearance does not seem to be significantly impacted by therapeutic hypothermia. Rather, lactic acidosis typically improves after an increase in oxygenation and the restoration of circulation.

**Educational objective:**

Neuronal damage after hypoxic-ischemic injury is often related to the formation of reactive oxygen species, which mediate widespread cellular damage. Therapeutic hypothermia decreases the formation of reactive oxygen species by decreasing cellular metabolism and slowing reperfusion.

**References**

- Therapeutic hypothermia: critical review of the molecular mechanisms of action.

| Pathophysiology | Nervous System | Anoxic brain injury |
|---|---|---|
| Subject | System | Topic |



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A new inhaled anesthetic under development by a pharmaceutical company is tested in a series of experiments to determine its pharmacokinetic properties. During one of the experiments, the anesthetic agent is administered at a constant partial pressure while arterial and venous concentrations are monitored. The study results show that the anesthetic has a very large arteriovenous concentration gradient shortly after beginning inhalation. Which of the following best describes the properties of the new anesthetic?

A. Fast equilibration with the brain
B. Low peripheral tissue solubility
C. Low peripheral tissue uptake
D. Low potency
E. Slow onset of action

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A new inhaled anesthetic under development by a pharmaceutical company is tested in a series of experiments to determine its pharmacokinetic properties. During one of the experiments, the anesthetic agent is administered at a constant partial pressure while arterial and venous concentrations are monitored. The study results show that the anesthetic has a very large arteriovenous concentration gradient shortly after beginning inhalation. Which of the following best describes the properties of the new anesthetic?

A. Fast equilibration with the brain (35%)
B. Low peripheral tissue solubility (14%)
C. Low peripheral tissue uptake (11%)
D. ~~Low potency~~ (10%)
E. Slow onset of action (28%)

Correct

28%
Answered correctly

02 mins, 22 secs
Time Spent

01/12/2021
Last Updated



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Before gas anesthetics can reach the target organ (brain), they must move through a number of compartments (inhaled air → lungs → blood→ brain). The onset of anesthesia occurs when a sufficient quantity of anesthetic is transferred to the brain. The factors shown in the table influence the rate of transfer of anesthetic through the compartments and determine the onset of action.

**Factors influencing anesthetic concentration**

| Compartment | Determinants of anesthetic concentration | Effect |
|---|---|---|
| Inhaled air | The partial pressure (ie, tension) of the anesthetic in the inspired gas | Anesthetic tension throughout the body will eventually equilibrate with its tension in the inspired air. When this occurs, the tissues are said to become saturated. |
| Lungs | Pulmonary ventilation rate | The rate of rise of gas tension in alveoli is directly proportional to both the rate & depth of respiration. |
| Blood | Solubility of the anesthetic in the blood (blood/gas partition coefficient) | Higher blood solubility means that more anesthetic must be absorbed by the blood before it can be effectively transferred to |


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Exhibit Display

**Factors influencing anesthetic concentration**

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| Lungs | Pulmonary ventilation rate | The rate of rise of gas tension in alveoli is directly proportional to both the rate & depth of respiration. |
| Blood | Solubility of the anesthetic in the blood (blood/gas partition coefficient) | Higher blood solubility means that more anesthetic must be absorbed by the blood before it can be effectively transferred to other tissues. |
| Target organ (brain) | Solubility of the anesthetic in the peripheral tissues negatively affects brain saturation. | Higher peripheral tissue solubility means more anesthetic is extracted from the arterial blood. This increases the arteriovenous concentration gradient, meaning that more anesthetic must be absorbed to saturate the blood & then the brain. |

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coefficient) before it can be effectively transferred to



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The arteriovenous concentration gradient is the difference between the concentration of a gas anesthetic in arterial and venous blood. The solubility of the anesthetic in the peripheral tissues is a major factor in determining the size of the arteriovenous gradient. If tissue solubility is high, a large amount of anesthetic is taken up from arterial blood, which results in low venous concentration. As a result, saturation of the blood requires further absorption of anesthetic in order to replace that which is absorbed by the peripheral tissues. Because blood saturation takes longer, brain saturation is also delayed and onset of action is slower.

In contrast, anesthetic gases with low peripheral tissue solubility have smaller arteriovenous gradients as there is less peripheral tissue uptake **(Choices B and C)**. Less anesthetic is required to replace the amount absorbed by the peripheral tissue and so blood saturation occurs quickly, allowing concentrations in the brain to equilibrate faster **(Choice A)**.

**(Choice D)** Potency of the anesthetic is defined by the minimal alveolar concentration (MAC), the alveolar concentration that prevents movement in 50% of patients exposed to noxious stimuli. Potent anesthetics have low MACs. The arteriovenous concentration gradient influences the rate of induction, not anesthetic potency.

**Educational objective:**


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In contrast, anesthetic gases with low peripheral tissue solubility have smaller arteriovenous gradients as there is less peripheral tissue uptake **(Choices B and C)**. Less anesthetic is required to replace the amount absorbed by the peripheral tissue and so blood saturation occurs quickly, allowing concentrations in the brain to equilibrate faster **(Choice A)**.

**(Choice D)** Potency of the anesthetic is defined by the minimal alveolar concentration (MAC), the alveolar concentration that prevents movement in 50% of patients exposed to noxious stimuli. Potent anesthetics have low MACs. The arteriovenous concentration gradient influences the rate of induction, not anesthetic potency.

**Educational objective:**
The arteriovenous concentration gradient reflects the overall tissue solubility of an anesthetic. Anesthetics with high tissue solubility are characterized by large arteriovenous concentration gradients and slower onsets of action.

| Pharmacology | Nervous System | Anesthesia |
|---|---|---|
| Subject | System | Topic |

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A 15-year-old boy is brought to the office by his mother due to difficulty with movement. The patient enjoys playing high school basketball but had to leave the team this year due to his progressively worsening symptoms. On examination, he is found to have significant kyphoscoliosis and a high plantar arch. His older brother suffered from a neurologic disorder and died of heart failure at age 25. This patient most likely has which of the following neuropathologic findings?

A. Atrophy of the caudate nucleus
B. Cerebral cortex atrophy
C. Degeneration of the spinocerebellar tracts
D. Demyelination of peripheral nerves
E. Loss of neurons in the anterior horn of the spinal cord
F. Loss of neurons in the substantia nigra

Submit


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A. ~~Atrophy of the caudate nucleus~~ (5%)

B. ~~Cerebral cortex atrophy~~ (3%)

C. Degeneration of the spinocerebellar tracts (62%)

D. ~~Demyelination of peripheral nerves~~ (12%)

E. ~~Loss of neurons in the anterior horn of the spinal cord~~ (15%)

F. Loss of neurons in the substantia nigra (1%)

Correct

62% Answered correctly

01 min, 08 secs Time Spent

11/20/2020 Last Updated



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Correct

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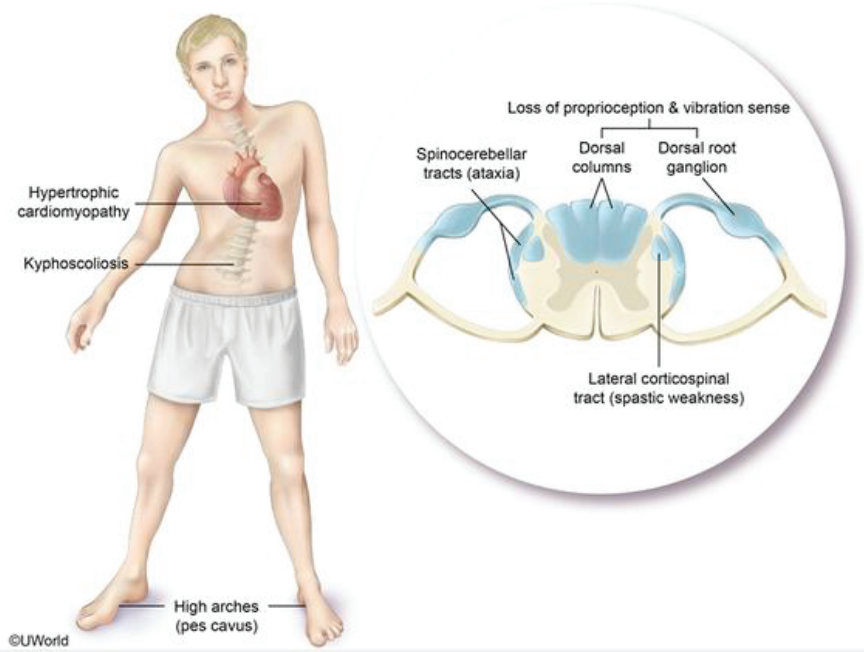
## Friedreich ataxia

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**Friedreich ataxia** is an autosomal recessive disorder caused by mutation of the frataxin (*FXN*) gene. This gene codes for an essential mitochondrial protein involved in the assembly of iron-sulfur enzymes. An increased number of trinucleotide repeats (GAA) is present in the mutated gene, causing decreased *FXN* expression. This leads to decreased mitochondrial energy production and increased oxidative stress, resulting in degeneration of neural tracts and peripheral nerves. The following sites of involvement are characteristic:

1. Spinocerebellar and lateral corticospinal tract degeneration causes **gait ataxia** and spastic muscle weakness, respectively.
2. Degeneration of the dorsal columns and dorsal root ganglia causes **loss of position and vibration** sensation.
3. **Kyphoscoliosis and foot abnormalities** (pes cavus) are characteristic skeletal deformities.
4. Heart involvement includes **hypertrophic cardiomyopathy** and congestive heart failure.
5. **Diabetes mellitus** develops in about 10% of patients with Friedreich ataxia.

**(Choice A)** Huntington disease is an autosomal dominant disorder caused by trinucleotide repeats (CAG) in the huntingtin (*HTT*) gene, which results in severe neuronal loss in the caudate nucleus. This condition manifests with dementia, behavioral abnormalities, and choreiform movements.


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**(Choice B)** Cerebral cortex atrophy occurs in Alzheimer and Pick diseases. Alzheimer disease is characterized by diffuse, mild cortical atrophy and progressive memory loss. Pick disease causes pronounced frontotemporal atrophy, illustrated by behavioral and emotional abnormalities.

**(Choice D)** Charcot-Marie-Tooth disease is an autosomal dominant disorder associated with demyelination of peripheral nerves. Typical findings include distal leg weakness/atrophy with sensory deficits, pes cavus, and kyphoscoliosis; cardiomyopathy is not characteristic.

**(Choice E)** Loss of neurons in the anterior horn of the spinal cord occurs in poliomyelitis and leads to flaccid paralysis, atrophy, areflexia, and muscle fasciculations. Damage of these neurons also occurs in amyotrophic lateral sclerosis.

**(Choice F)** Loss of neurons of the substantia nigra occurs in Parkinson disease, which manifests with bradykinesia, rigidity, and a resting "pill-rolling" tremor.

**Educational objective:**
Friedreich ataxia is characterized by cerebellar ataxia (spinocerebellar tract degeneration) and loss of position/vibration sensation (dorsal column/dorsal root ganglia degeneration), kyphoscoliosis, and hypertrophic cardiomyopathy. Foot abnormalities and diabetes mellitus are also common.


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A newborn is examined in the delivery room shortly after being born vaginally to a 38-year-old woman. The mother had intermittent prenatal care, and the pregnancy was complicated by bipolar disorder and chronic hypertension. Interview of the mother reveals pressured and tangential speech. She states, "I take my prescribed meds when I remember," and then adds, "I have a good memory, and I took the meds most of the time throughout the pregnancy." She claims to have smoked cigarettes occasionally but then changes the subject when asked if other substances were used during pregnancy. Examination of the neonate shows a nondysmorphic face and a mass overlying the lower spine that is covered with a patch of hair. Which of the following maternal interventions could have most likely prevented this neonate's abnormalities?

A. Antenatal steroid therapy
B. Avoiding alcohol consumption
C. Increasing dose of mood stabilizer
D. Lowering dose of antihypertensive drug
E. Smoking cessation


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E. Smoking cessation
F. Vitamin supplementation


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A. ~~Antenatal steroid therapy~~ (0%)
B. Avoiding alcohol consumption (3%)
C. Increasing dose of mood stabilizer (0%)
D. ~~Lowering dose of antihypertensive drug~~ (0%)
E. Smoking cessation (1%)
✓ F. Vitamin supplementation (93%)

Correct
93%
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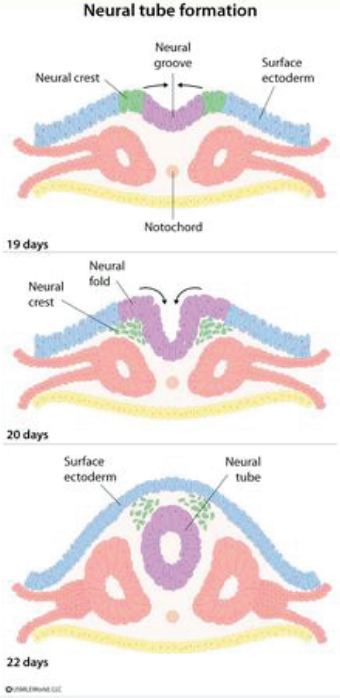


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Midline fusion of neural folds creates the neural tube during the third week of fetal life. The neural tube is a structure that is connected to the amniotic cavity by openings at the ends known as anterior and posterior neuropores. Failure of neuropore closure by 4 weeks gestation leads to **neural tube defects** (NTDs). Anterior NTDs include anencephaly (absence of the forebrain) and encephalocele (protrusion of neural tissue through the cranial defect). Posterior NTDs include spina bifida occulta, meningocele, and meningomyelocele. Meningocele and meningomyelocele present as a **cystic mass at the lower spine** that is covered with skin and sometimes a **tuft of hair** (seen in this patient). A meningocele consists of spinal meninges that protrude through the vertebral arch defect. A meningomyelocele has portions of the spinal cord or cauda equina within the protruding meningeal sac.

**Folate (vitamin $B_9$)** supplementation reduces risk of NTDs and is recommended for all women of childbearing age because the neural tube develops during the time when most women are unaware of their pregnancy. Prenatal **valproate** use for **bipolar disorder** (likely in this patient) or **epilepsy** is associated with a 10- to 20-fold increased risk of NTDs due to impaired folate metabolism. Other risk factors include maternal use of folate antagonists (eg, methotrexate, trimethoprim-sulfamethoxazole).

**(Choice A)** Antenatal steroid therapy (eg, betamethasone) reduces the incidence of neonatal respiratory



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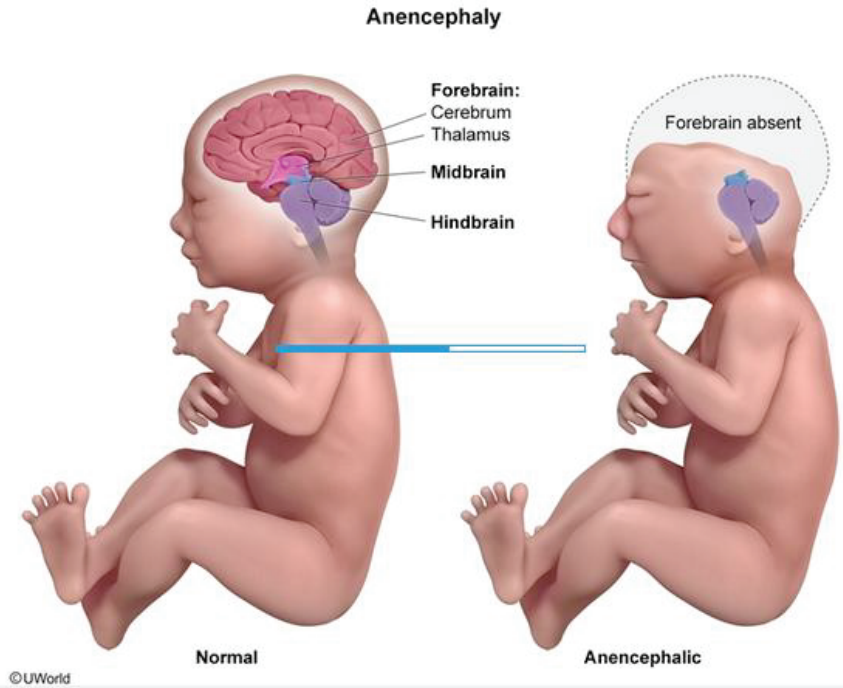


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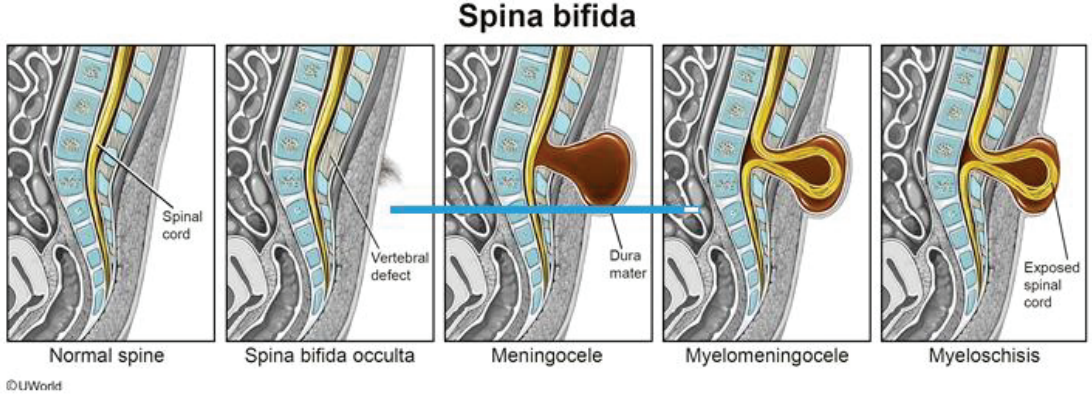


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**(Choice A)** Antenatal steroid therapy (eg, betamethasone) reduces the incidence of neonatal respiratory distress syndrome in premature infants. It does not reduce the risk of NTDs.

**(Choice B)** Although chronic alcohol consumption can result in folate deficiency (and therefore NTDs), it is more commonly associated with fetal alcohol syndrome. However, fetal alcohol syndrome is unlikely in the absence of short palpebral fissures, a thin vermilion border, and a smooth philtrum.

**(Choice C)** Lithium and valproate are first-line drugs for acute mania. If valproate cannot be substituted by another drug to control a mood or epilepsy disorder, the lowest effective dose should be prescribed during pregnancy. Lithium use in pregnancy is also not recommended due to its association with increased incidence of Ebstein anomaly.

**(Choices D and E)** Uncontrolled hypertension and tobacco use can cause fetal growth restriction, premature delivery, and placental abruption. Tobacco use, hypertension, and antihypertensive medications are not associated with NTDs.

**Educational objective:**
Failure of neural tube closure at 4 weeks gestation results in neural tube defects (NTDs). First trimester use of valproate is a significant risk factor for NTDs, but periconceptional folate (vitamin $B_9$) supplementation reduces this risk.


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**(Choice A)** Antenatal steroid therapy (eg, betamethasone) reduces the incidence of neonatal respiratory

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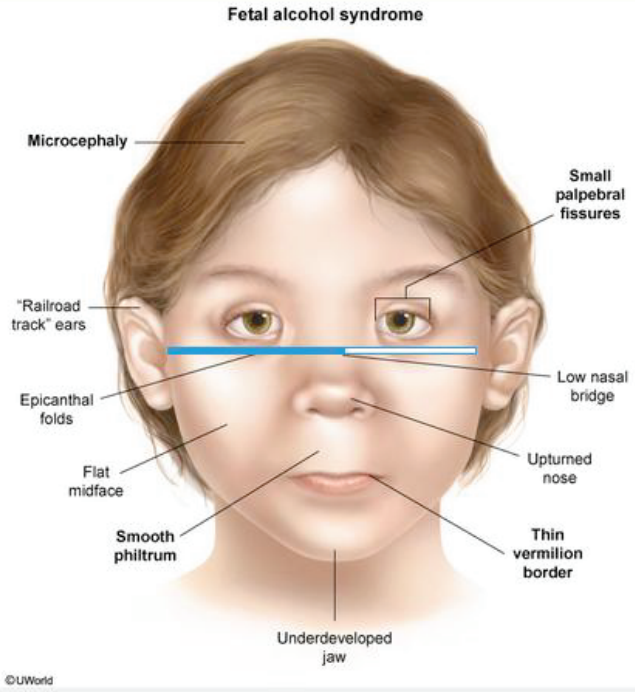


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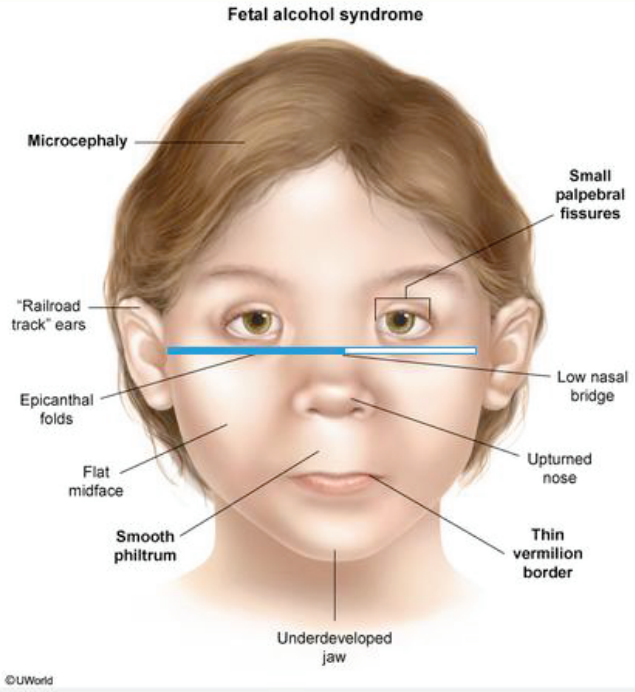


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(Choice A) Antenatal steroid therapy (eg, betamethasone) reduces the incidence of neonatal respiratory

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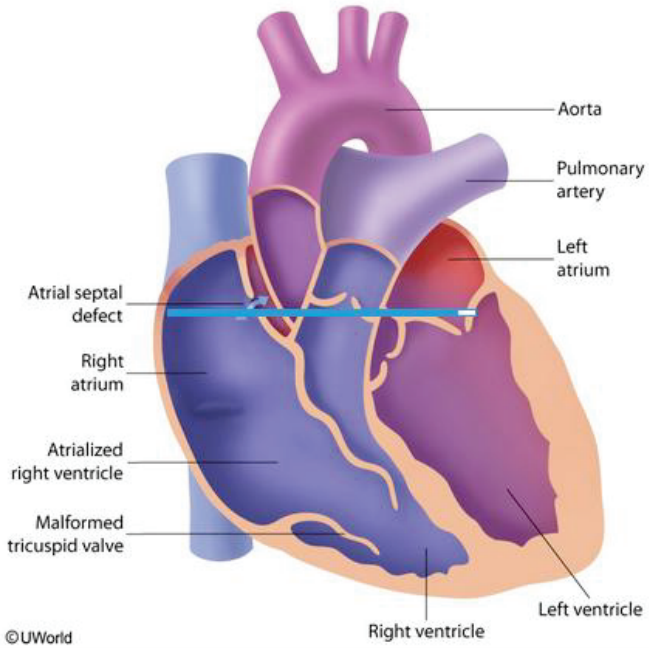
Ebstein's anomaly

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(Choice A) Antenatal steroid therapy (eg, betamethasone) reduces the incidence of neonatal respiratory

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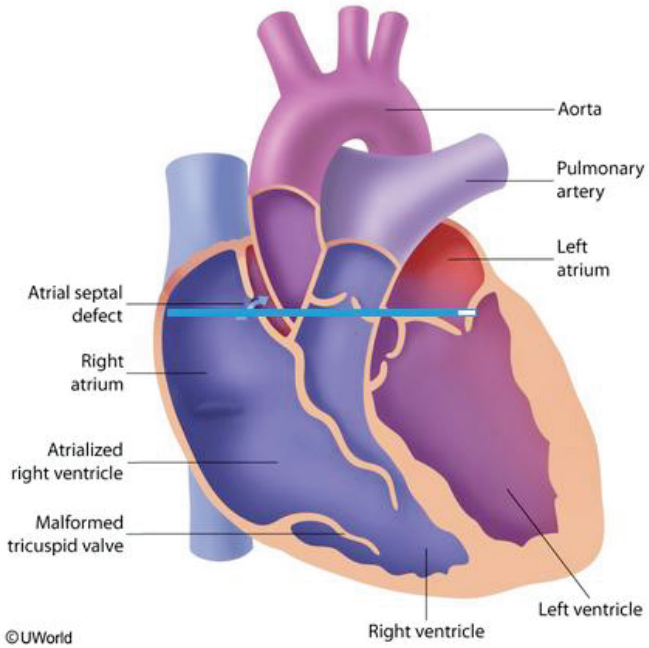
Ebstein's anomaly

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A 46-year-old man experiences burning pain in his left thigh and leg. The next day, he notices groups of erythematous, tender, fluid-filled vesicles in the painful region. The lesions gradually crust over the next several days as shown in the exhibit. Which of the following dermatomes are most likely involved in this patient's disease process?

- A. L1-L2
- B. L3-L4
- C. L5-S1
- D. S2-S3
- E. No specific dermatome pattern

Submit



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A. L1-L2 (10%)
B. L3-L4 (69%)
C. ~~L5-S1~~ (11%)
D. ~~S2-S3~~ (3%)
E. ~~No specific dermatome pattern~~ (4%)

Correct

69%
Answered correctly

01 min, 01 sec
Time Spent

02/15/2021
Last Updated

Explanation



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Correct

69%
Answered correctly

01 min, 01 sec
Time Spent

02/15/2021
Last Updated

Explanation



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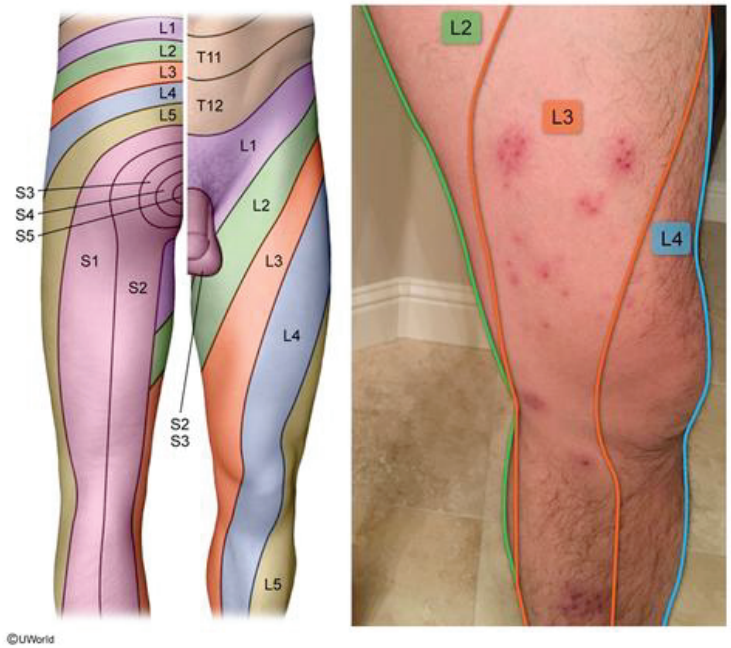
Zoster dermatomal distribution

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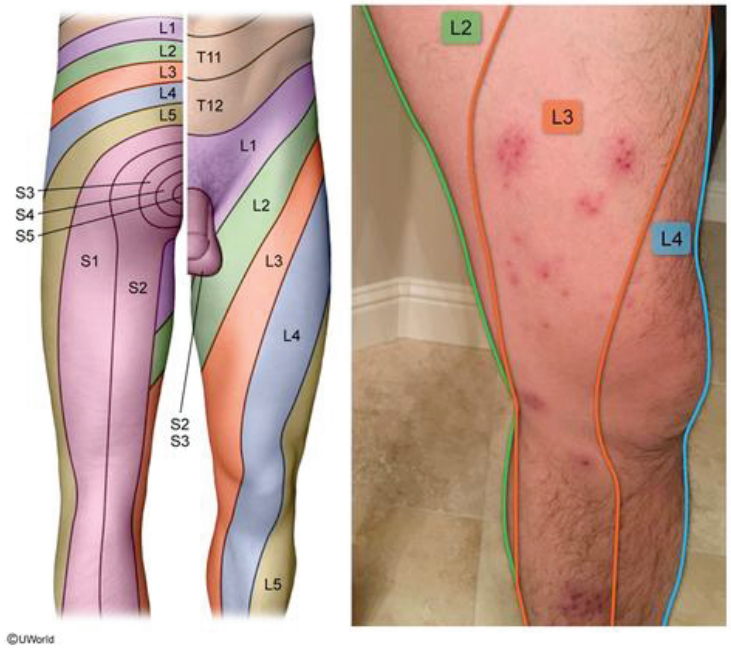


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This patient has single and grouped vesicles in various stages of ulceration and crusting, which is consistent with **herpes zoster** (ie, shingles). Following primary VZV infection (ie, chickenpox), the virus migrates via sensory nerves to the **dorsal spinal ganglia**, where it lies dormant for years. Reactivation of the virus typically occurs in a single (or multiple-adjacent) ganglion. This causes hemorrhagic inflammation involving the entire peripheral nerve associated with that ganglion and eruption of a painful, vesicular rash on the skin supplied by that sensory nerve (ie, dermatome).

This patient's vesicular rash primarily involves the **anteromedial thigh** and **medial leg**, which is consistent with the dermatomal distribution of **L3 and L4**.

**(Choice A)** The L1 dermatome is at the level of the inguinal ligament. The L2 dermatome covers the upper anteromedial thigh but does not extend downward into the leg.

**(Choice C)** The L5 dermatome covers the lateral thigh and anterolateral leg along with the dorsum/sole of the foot. The S1 dermatome includes the posterior thigh and leg and the lateral portion of the foot.

**(Choice D)** The S2 dermatome supplies portions of the posterior thigh and leg as well as the perineum. S3 primarily supplies the perineum.

**(Choice E)** Primary VZV infection (ie, chickenpox) produces a generalized vesicular rash. However,


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**(Choice A)** The L1 dermatome is at the level of the inguinal ligament. The L2 dermatome covers the upper anteromedial thigh but does not extend downward into the leg.

**(Choice C)** The L5 dermatome covers the lateral thigh and anterolateral leg along with the dorsum/sole of the foot. The S1 dermatome includes the posterior thigh and leg and the lateral portion of the foot.

**(Choice D)** The S2 dermatome supplies portions of the posterior thigh and leg as well as the perineum. S3 primarily supplies the perineum.

**(Choice E)** Primary VZV infection (ie, chickenpox) produces a generalized vesicular rash. However,


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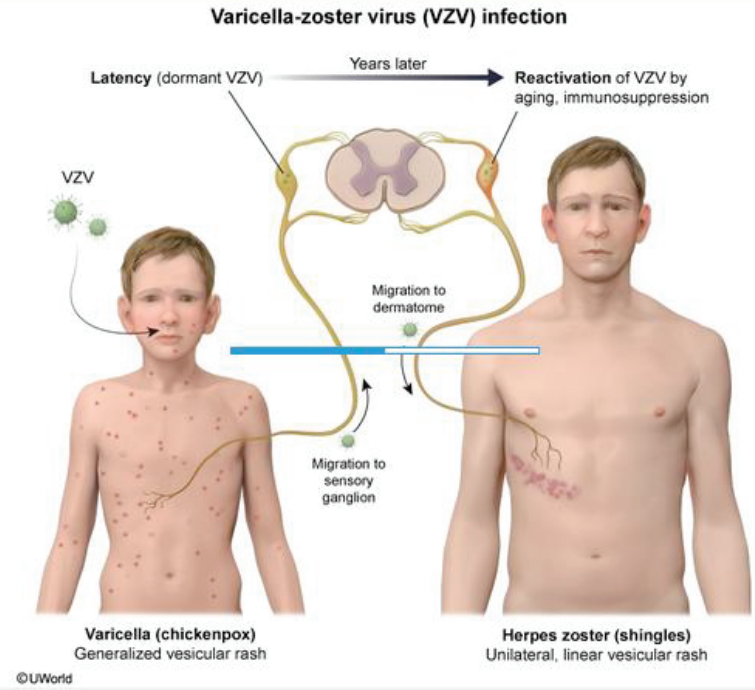


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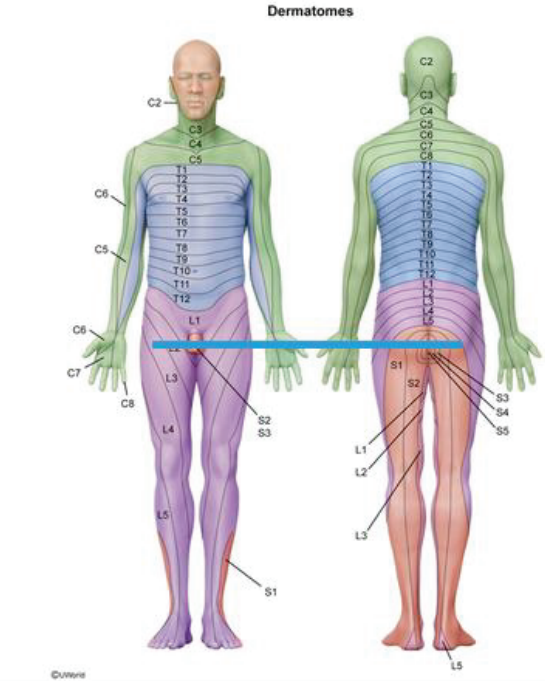


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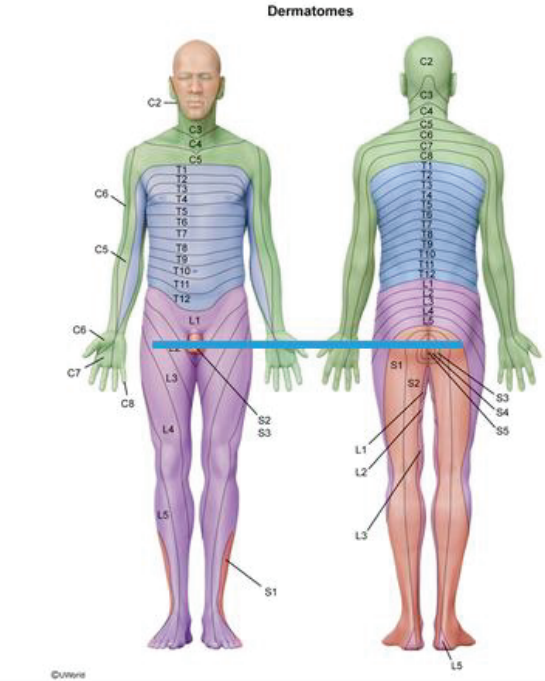


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**(Choice D)** The S2 dermatome supplies portions of the posterior thigh and leg as well as the perineum. S3 primarily supplies the perineum.

**(Choice E)** Primary VZV infection (ie, chickenpox) produces a generalized vesicular rash. However, reactivation typically occurs in a single (or multiple-adjacent) spinal ganglia, leading to a rash confined to the distribution of those nerves (ie, dermatome).

**Educational objective:**
Herpes zoster reactivation typically occurs in a single or multiple-adjacent dorsal spinal ganglia, leading to a vesicular rash in a dermatomal distribution. The L3 and L4 dermatomes supply the anteromedial thigh and medial leg.

| Anatomy | Nervous System | Herpes zoster |
|---|---|---|
| Subject | System | Topic |

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Herpes zoster reactivation typically occurs in a single or multiple-adjacent dorsal spinal ganglia, leading to a vesicular rash in a dermatomal distribution. The L3 and L4 dermatomes supply the anteromedial thigh and medial leg.

| Anatomy | Nervous System | Herpes zoster |
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A 5-year-old boy has developed persistent food-seeking behavior over the past few months. His mother initially thought that the boy was undergoing a growth spurt, but despite how much she fed him he never seemed satisfied. He has gained more than 4.5 kg (10 lb). The patient has also started complaining of a headache and nausea in the morning. His physical examination is significant for BMI of 32 kg/m$^2$. Temperature is 37.2 C (99 F), blood pressure is 100/70 mm Hg, pulse is 92/min, and respirations are 16/min. His pediatrician becomes concerned about possible central nervous system involvement. This patient's food-seeking behavior could be explained by a lesion causing impairment of which hypothalamic nucleus?

A. Anterior
B. Lateral
C. Posterior
D. Suprachiasmatic
E. Supraoptic
F. Ventromedial



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seemed satisfied. He has gained more than 4.5 kg (10 lb). The patient has also started complaining of a headache and nausea in the morning. His physical examination is significant for BMI of 32 kg/m$^2$. Temperature is 37.2 C (99 F), blood pressure is 100/70 mm Hg, pulse is 92/min, and respirations are 16/min. His pediatrician becomes concerned about possible central nervous system involvement. This patient's food-seeking behavior could be explained by a lesion causing impairment of which hypothalamic nucleus?

- A. ~~Anterior~~ (5%)
- B. Lateral (20%)
- C. ~~Posterior~~ (3%)
- D. ~~Suprachiasmatic~~ (2%)
- E. ~~Supraoptic~~ (1%)
- ✓ F. Ventromedial (66%)

Correct

66%
Answered correctly

01 min, 19 secs
Time Spent

10/05/2020
Last Updated



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| Major functions of hypothalamic nuclei | |
|---|---|
| **Ventromedial** | Mediates satiety; destruction leads to hyperphagia |
| **Lateral** | Mediates hunger; destruction leads to anorexia |
| **Anterior** | Mediates heat dissipation; destruction leads to hyperthermia |
| **Posterior** | Mediates heat conservation; destruction leads to hypothermia |
| **Arcuate** | Secretion of dopamine (inhibits prolactin), GHRH |
| **Medial preoptic** | Secretion of GnRH, regulates sexual behavior |
| **Paraventricular** | Secretion of oxytocin, CRH, TRH & small amounts of ADH |
| **Supraoptic** | Secretion of ADH & small amounts of oxytocin |
| **Suprachiasmatic** | Circadian rhythm regulation & pineal gland function |

ADH = antidiuretic hormone; CRH = corticotropin-releasing hormone; GHRH = growth hormone-releasing hormone; GnRH = gonadotropin-releasing hormone; TRH = thyrotropin-releasing hormone.


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hormone.

The **hypothalamus** is in the diencephalon at the base of the brain. It is a key region involved in **homeostasis**; including the regulation of temperature, appetite, emotion, growth, and circadian rhythm. The ventromedial and lateral nuclei are involved in the regulation of food intake.

The **ventromedial nucleus** is vital in monitoring blood glucose and **mediates satiety**. Lesions of this area of the hypothalamus (eg, trauma, infection, brain tumors) can result in **hyperphagia and obesity**. Conversely, the lateral nucleus signals hunger. Lesions can result in loss of appetite (eg, failure to thrive) **(Choice B)**.

**(Choices A and C)** The anterior and posterior nuclei are involved in temperature control through regulation of the autonomic nervous system. The anterior nucleus coordinates cooling via inhibition of adrenergic input, causing vasodilation and stimulation of cholinergic pathways (eg, sweating). Destruction of this nucleus can cause uncontrolled hyperthermia. Conversely, the posterior nucleus regulates heat conservation and heat production via vasoconstriction and shivering. Destruction can lead to hypothermia.

**(Choice D)** The suprachiasmatic nucleus is located immediately above the optic chiasm and receives visual input directly from the retina. It helps regulate circadian rhythms by relaying light information to other hypothalamic nuclei and to the pineal gland.



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of this nucleus can cause uncontrolled hyperthermia. Conversely, the posterior nucleus regulates heat conservation and heat production via vasoconstriction and shivering. Destruction can lead to hypothermia.

**(Choice D)** The suprachiasmatic nucleus is located immediately above the optic chiasm and receives visual input directly from the retina. It helps regulate circadian rhythms by relaying light information to other hypothalamic nuclei and to the pineal gland.

**(Choice E)** The supraoptic and paraventricular nuclei project axons into the posterior pituitary gland (neurohypophysis), producing vasopressin (antidiuretic hormone) and oxytocin. Oxytocin is associated with uterine contractions and milk letdown; vasopressin regulates fluid balance via reabsorption of water from the kidneys.

**Educational objective:**

The hypothalamus is a key region responsible for homeostasis. The ventromedial nucleus mediates satiety; lesions of this area of the hypothalamus can result in hyperphagia and obesity.

**References**


- Role of ventromedial hypothalamus in high fat diet induced obesity in male rats: association with lipid profile, thyroid profile and insulin resistance.
- Metabolic mystery: aging, obesity, diabetes, and the ventromedial hypothalamus.




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A 21-year-old man is brought to the emergency department by his mother after she found him violently shaking on the kitchen floor of her home. The patient urinated on himself and bit his tongue during the incident. He has a past medical history of posttraumatic epilepsy and is noncompliant with his antiseizure medications. In the hospital, he has several brief, back-to-back generalized tonic-clonic seizures and never fully regains consciousness between episodes. Intravenous lorazepam 2 mg is administered, and the seizures stop. Intravenous infusion of another drug is started simultaneously to prevent seizure recurrence. Which of the following is the most likely mechanism of action of the second drug infused in this patient?

A. Decreases calcium current in thalamic neurons
B. Decreases sodium current in cortical neurons
C. Dose-dependent activation of postsynaptic $GABA_A$ receptors
D. Increases postsynaptic chloride influx
E. Irreversible inhibition of GABA catabolism in the central nervous system


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shaking on the kitchen floor of her home. The patient urinated on himself and bit his tongue during the incident. He has a past medical history of posttraumatic epilepsy and is noncompliant with his antiseizure medications. In the hospital, he has several brief, back-to-back generalized tonic-clonic seizures and never fully regains consciousness between episodes. Intravenous lorazepam 2 mg is administered, and the seizures stop. Intravenous infusion of another drug is started simultaneously to prevent seizure recurrence. Which of the following is the most likely mechanism of action of the second drug infused in this patient?

A. Decreases calcium current in thalamic neurons (5%)

✓ B. Decreases sodium current in cortical neurons (66%)

C. Dose-dependent activation of postsynaptic $GABA_A$ receptors (12%)

D. Increases postsynaptic chloride influx (10%)

E. Irreversible inhibition of GABA catabolism in the central nervous system (4%)

Correct

66%

01 min, 20 secs

11/16/2020



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| Mechanisms of common antiseizure drugs | |
|---|---|
| **Phenytoin** | Blocks $Na^+$ channels |
| **Carbamazepine** | |
| **Valproic acid** | Blocks $Na^+$ channels & ↑ GABA levels |
| **Benzodiazepine** | ↑ $GABA_A$ action |
| **Phenobarbital** | |
| **Levetiracetam** | Modulates GABA & glutamate release |
| **Ethosuximide** | Blocks thalamic T-type $Ca^{2+}$ channels |

**Status epilepticus** is a single seizure lasting >5 minutes or the occurrence of multiple discrete seizures with incomplete recovery of consciousness between episodes. Common causes include structural brain injury (eg, stroke, tumor, head trauma), infection, metabolic abnormalities (eg, hypoglycemia), and medication noncompliance in individuals with known epilepsy. Prompt evaluation and treatment is necessary as the condition is life-threatening and associated with a number of systemic complications (eg,


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medication noncompliance in individuals with known epilepsy. Prompt evaluation and treatment is necessary as the condition is life-threatening and associated with a number of systemic complications (eg, cardiac arrhythmias, hypoventilation/hypoxia, disabling neurologic deficits).

Intravenous **lorazepam** is a benzodiazepine that potentiates the effects of the inhibitory neurotransmitter GABA in the central nervous system. It is the initial drug of choice for treatment of status epilepticus due to its efficacy and rapid onset of action. Intravenous **phenytoin** (or fosphenytoin) is a long-acting anticonvulsant that is administered **concurrently** to prevent the recurrence of seizure activity, regardless of patient responsiveness to lorazepam. Phenytoin inhibits neuronal high-frequency firing in the cortex by reducing the ability of **sodium channels** to recover from inactivation.

**(Choice A)** Ethosuximide blocks T-type calcium channels in thalamic neurons. It is a first-line treatment for absence seizures.

**(Choices C and D)** Benzodiazepines and barbiturates (eg, phenobarbital) bind to the ligand-gated chloride channel of the $GABA_A$ receptor. These substances enhance the inhibitory effect of GABA by increasing postsynaptic chloride influx.

**(Choice E)** Vigabatrin is an irreversible inhibitor of GABA transaminase, the enzyme responsible for GABA catabolism in the central nervous system. Vigabatrin is one of several drugs that can be used in cases of


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**(Choice A)** Ethosuximide blocks T-type calcium channels in thalamic neurons. It is a first-line treatment for absence seizures.

**(Choices C and D)** Benzodiazepines and barbiturates (eg, phenobarbital) bind to the ligand-gated chloride channel of the $GABA_A$ receptor. These substances enhance the inhibitory effect of GABA by increasing postsynaptic chloride influx.

**(Choice E)** Vigabatrin is an irreversible inhibitor of GABA transaminase, the enzyme responsible for GABA catabolism in the central nervous system. Vigabatrin is one of several drugs that can be used in cases of treatment-resistant epilepsy.

**Educational objective:**
Status epilepticus is a single seizure lasting >5 minutes or the occurrence of multiple discrete seizures with incomplete recovery of consciousness between episodes. The initial treatment includes intravenous lorazepam and phenytoin given concurrently. Phenytoin is a long-acting anticonvulsant that inhibits neuronal high-frequency firing by reducing the ability of sodium channels to recover from inactivation.

**References**

- The management of status epilepticus.
- Basis of the antiseizure action of phenytoin.


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www.ncbi.nlm.nih.gov/pubmed/11385046

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A 28-year-old man is found unresponsive by his roommate. The roommate states the patient returned late last night after a party, and this morning he was unable to wake the patient up. Paramedics find the patient without respirations and pulse and declare him dead. Autopsy examination shows hemorrhage in the basal ganglia and midbrain that extends into the third ventricle. There is no arteriosclerosis or fibrinoid necrosis of the arterioles. Scattered areas of infarcted subendocardial myocardium are also seen. A substance with which of the following synaptic effects most likely predisposed this patient to death?

A. Blockade of postsynaptic neurotransmitter receptor
B. Decreased metabolism of released neurotransmitter
C. Impaired presynaptic neurotransmitter reuptake
D. Increased release of neurotransmitter vesicles
E. Increased synthesis of presynaptic neurotransmitter

Submit



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A 28-year-old man is found unresponsive by his roommate. The roommate states the patient returned late last night after a party, and this morning he was unable to wake the patient up. Paramedics find the patient without respirations and pulse and declare him dead. Autopsy examination shows hemorrhage in the basal ganglia and midbrain that extends into the third ventricle. There is no arteriosclerosis or fibrinoid necrosis of the arterioles. Scattered areas of infarcted subendocardial myocardium are also seen. A substance with which of the following synaptic effects most likely predisposed this patient to death?

- A. Blockade of postsynaptic neurotransmitter receptor (6%)
- B. Decreased metabolism of released neurotransmitter (9%)
- ✓ C. Impaired presynaptic neurotransmitter reuptake (65%)
- D. Increased release of neurotransmitter vesicles (16%)
- E. Increased synthesis of presynaptic neurotransmitter (2%)

Correct

Collecting Statistics

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03/16/2021
Last Updated



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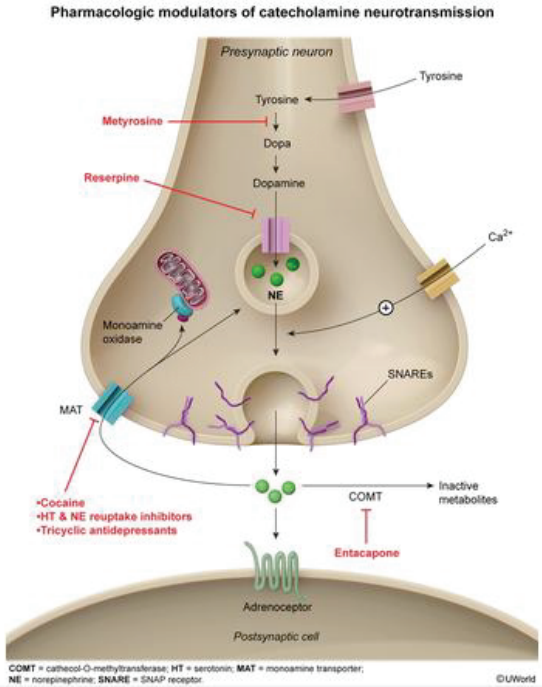


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This young man who experienced sudden, unexpected death and has autopsy evidence of a large hemorrhagic stroke and scattered myocardial infarction most likely experienced **cocaine toxicity**. The cardiovascular effects of cocaine toxicity result from **impaired reuptake of catecholamine neurotransmitters**, including norepinephrine and dopamine, due to inhibition of the presynaptic monoamine transporter. Cocaine toxicity can cause **stroke** via the following mechanisms:

- Stimulation of **cerebral artery vasospasm** primarily via increased levels of intrasynaptic dopamine.
- **Blood pressure is increased** via both vasoconstriction and **increased sympathetic tone** (ie, increased contractility and heart rate), encouraging **dissection** of large cerebral arteries and **rupture** of small **cerebral vessels**. This allows lacunar infarcts to occur in young patients (in the absence of the arteriosclerosis and fibrinoid necrosis that develop with prolonged hypertension and facilitate these infarcts in older patients).
- **Increased activation of platelets** and stimulation of prothrombotic mediators (eg, thromboxane) encourage thrombus formation.

In the heart, similar effects combined with an increase in myocardial oxygen demand (due to increased contractility, afterload, and heart rate) contribute to the propensity for **myocardial ischemia** and infarction.


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**(Choice A)** Beta blockers bind to postsynaptic adrenergic receptors and can prevent some of the cardiac effects of cocaine toxicity (the cardiac adrenergic response is primarily controlled by beta-1 receptors). However, beta blockers may worsen the alpha receptor–mediated vasoconstriction of cocaine toxicity (due to unopposed alpha stimulation) and are typically avoided.

**(Choice B)** Cathecol-O-methyltransferase (COMT) metabolizes catecholamines after they are released into the synapse. COMT inhibitors (eg, entacapone) are sometimes used to treat Parkinson disease (by slowing the breakdown of intrasynaptic dopamine).

**(Choices D and E)** Reserpine prevents the formation of presynaptic catecholamine vesicles, decreasing (rather than increasing) their release into the synapse. The medication is sometimes used to treat hypertension or agitated psychosis. Metyrosine, a tyrosine analogue and competitive inhibitor, decreases (rather than increases) the synthesis of presynaptic catecholamines. It is sometimes used to treat pheochromocytoma.

**Educational objective:**
Cocaine blocks the presynaptic reuptake of catecholamine neurotransmitters, including norepinephrine and dopamine. With cocaine toxicity, excessive postsynaptic stimulation by catecholamines can lead to arterial vasospasm and increased sympathetic drive, resulting in increased risk of stroke and myocardial infarction.



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A 23-year-old woman is referred to a neurologist due to recent-onset diplopia and ataxia. She has not had similar symptoms before. However, about a year ago, she experienced numbness and paresthesia involving her left leg that have since resolved. After a comprehensive neurological examination, the physician orders an MRI of the brain, which reveals several areas of T2 hyperintensity consistent with axonal demyelination. A diagnosis of multiple sclerosis is made. Which of the following neuronal properties is most likely to decrease as a direct result of demyelination?

A. Length (space) constant
B. Spatial summation
C. Temporal summation
D. Threshold
E. Time constant

Submit



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- A. Length (space) constant (45%)
- B. ~~Spatial summation~~ (9%)
- C. ~~Temporal summation~~ (16%)
- D. ~~Threshold~~ (2%)
- E. Time constant (24%)

Correct

45% Answered correctly

01 min, 52 secs Time Spent

11/12/2020 Last Updated



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Multiple sclerosis is an immune-mediated demyelinating disease of the central nervous system. Myelin is an electrical insulator and increases the conduction velocity of action potentials; demyelination leads to slowing of the impulses with resultant neurological deficits.

The speed of conduction down an axon depends on 2 constants: the length constant and the time constant (ie, **velocity = length/time**).

- The length constant, also known as the space constant, is a measure of how far along an axon an electrical impulse can propagate without requiring active regeneration by ion channels. It is based on the relative resistance of conduction along the axon (within the cytoplasm) compared to the resistance across the membrane. Myelin increases the length constant by reducing charge dissipation across the membrane (increasing membrane resistance). This allows the electrical impulse from individual sodium channels to travel farther, allowing activation of more distant channels. As such, demyelination will decrease the length constant and result in shorter impulse conduction.
- The time constant is a measure of the time it takes for the membrane potential to respond to a change in membrane permeability (ie, sodium channel activation) and is based on membrane resistance and capacitance. Myelin decreases membrane capacitance (reduces the amount of charge stored by the membrane) and increases membrane resistance (reduces charge leakage through the membrane) in


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Multiple sclerosis is an immune-mediated demyelinating disease of the central nervous system. Myelin is

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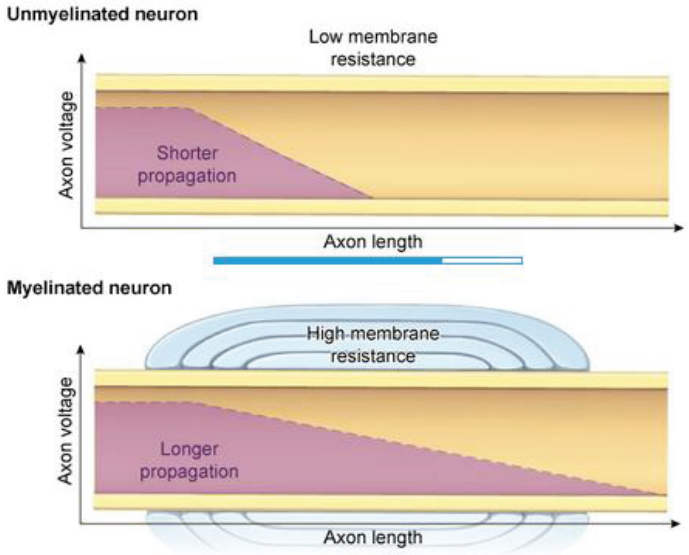
**Length constant of the neuron**

The distance an impulse can propagate depends on the membrane resistance compared to the axon (internal) resistance

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Multiple sclerosis is an immune-mediated demyelinating disease of the central nervous system. Myelin is

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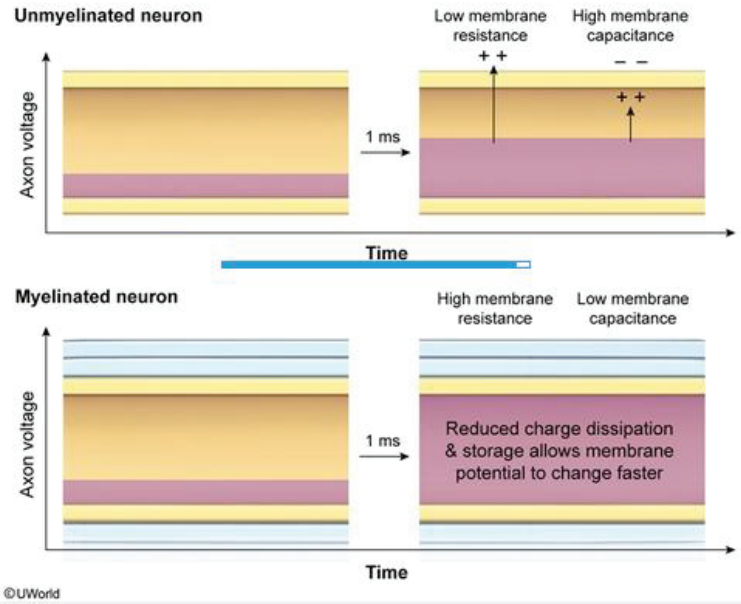
**Time constant of the neuron**

The time it takes for the membrane potential to change depends on both the membrane resistance and capacitance

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capacitance. Myelin decreases membrane capacitance (reduces the amount of charge stored by the membrane) and increases membrane resistance (reduces charge leakage through the membrane) in axon segments between the nodes of Ranvier; this reduces the time constant and allows the membrane potential to change faster. Demyelination would increase the time constant and result in slower changes in membrane voltage.

Therefore, **demyelination** decreases neuronal signaling velocity both by **decreasing the length constant** and increasing the time constant (ie, ↓ velocity = ↓ length / ↑ time) **(Choice E)**.

**(Choices B and C)** Summation refers to the additive effects of multiple postsynaptic potentials on a target neuron's membrane potential. Summation can occur in the dendrites, cell body, and axon hillock but not in the axon. Temporal summation refers to the combined effect of sequential impulses from the same neuron over time, whereas spatial summation refers to the combined effect of simultaneous impulses from several different neurons.

**(Choice D)** Threshold refers to the membrane potential value required to initiate an action potential. It is determined by the intrinsic properties of the voltage-gated sodium channels present in the membrane.

**Educational objective:**

The speed of conduction down an axon depends on 2 constants: the length constant and the time constant



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in membrane permeability (ie, sodium channel activation) and is based on membrane resistance and

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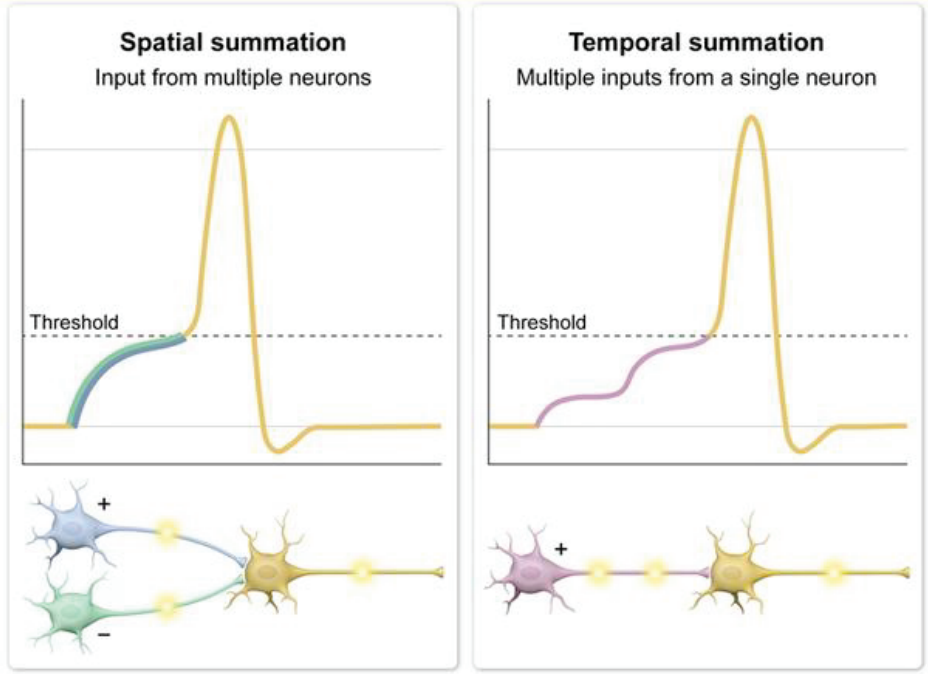


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The speed of conduction down an axon depends on 2 constants: the length constant and the time constant



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Therefore, **demyelination** decreases neuronal signaling velocity both by **decreasing the length constant** and increasing the time constant (ie, ↓ velocity = ↓ length / ↑ time) **(Choice E)**.

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**(Choice D)** Threshold refers to the membrane potential value required to initiate an action potential. It is determined by the intrinsic properties of the voltage-gated sodium channels present in the membrane.

**Educational objective:**

The speed of conduction down an axon depends on 2 constants: the length constant and the time constant (ie, velocity = length/time). Myelination increases the length constant and decreases the time constant, both of which improve axonal conduction speed. Demyelination thus impairs stimulus transmission.

**References**


- Multiple sclerosis: the disease and its manifestations.
- The pathophysiology of multiple sclerosis: the mechanisms underlying the production of symptoms and




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A 14-year-old boy presents with nausea, vomiting, generalized headache, ataxia, and visual complaints. The headaches have awoken him nightly for the past six weeks. MRI reveals a cystic tumor in the cerebellum. Biopsy of the tumor reveals a well-differentiated neoplasm comprised of spindle cells that have hair-like glial processes and are associated with microcysts. These cells are mixed with Rosenthal fibers and granular eosinophilic bodies. Based on these findings, the most likely diagnosis is which of the following?

A. Pilocytic Astrocytoma
B. Glioblastoma multiforme
C. Medulloblastoma
D. Ependymoma
E. Neuroblastoma

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www.ncbi.nlm.nih.gov/pubmed/11385046

A 14-year-old boy presents with nausea, vomiting, generalized headache, ataxia, and visual complaints. The headaches have awoken him nightly for the past six weeks. MRI reveals a cystic tumor in the cerebellum. Biopsy of the tumor reveals a well-differentiated neoplasm comprised of spindle cells that have hair-like glial processes and are associated with microcysts. These cells are mixed with Rosenthal fibers and granular eosinophilic bodies. Based on these findings, the most likely diagnosis is which of the following?

- ✓ A. Pilocytic Astrocytoma (71%)
- B. ~~Glioblastoma multiforme~~ (6%)
- ✗ C. Medulloblastoma (14%)
- D. ~~Ependymoma~~ (5%)
- E. ~~Neuroblastoma~~ (2%)

Incorrect
Correct answer
A

71%
Answered correctly

48 secs
Time Spent

01/30/2021
Last Updated



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www.ncbi.nlm.nih.gov/pubmed/11385046

Juvenile pilocytic astrocytomas usually arise in the cerebellum, brainstem, hypothalamic region, or optic pathways. Microscopically, pilocytic astrocytomas are well-differentiated neoplasms comprised of spindle cells with hair-like glial processes that are associated with microcysts. These cells are mixed with Rosenthal fibers and granular eosinophilic bodies.

**(Choice B)** GBMs occur most often in the subcortical white matter of the cerebral hemispheres. When a tumor in the frontal cortex spreads across the corpus callosum into the contralateral hemisphere, it creates the appearance of a bilateral symmetrical lesion, hence the term "butterfly glioma." GBMs are composed of poorly-differentiated, often-pleomorphic astrocytic cells with marked nuclear atypia and brisk mitotic activity. Necrosis is an essential diagnostic feature, and prominent microvascular proliferation is common.

**(Choice C)** Medulloblastoma (primitive neuroectodermal tumor, or PNET) is the second most common posterior fossa tumor in children. On microscopic examination, cells are small and poorly differentiated, with scant cytoplasm and little stroma. A high mitotic index is common. Classic Homer-Wright rosettes can be seen in one fifth of cases.

**(Choice D)** Ependymomas account for 10% of posterior fossa tumors in children. Intracranial lesions usually occur infratentorially, arising from the roof of the fourth ventricle in children, while spinal ependymomas typically occur in adults. Histologically, ependymal pseudorosettes with glial fibrillary acidic



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be seen in one fifth of cases.

**(Choice D)** Ependymomas account for 10% of posterior fossa tumors in children. Intracranial lesions usually occur infratentorially, arising from the roof of the fourth ventricle in children, while spinal ependymomas typically occur in adults. Histologically, ependymal pseudorosettes with glial fibrillary acidic protein (GFAP)–positive processes tapering toward blood vessels characterize ependymomas.

**(Choice E)** Neuroblastomas are the most common extracranial solid tumors occurring in children. Undifferentiated neuroblastomas are small, round, blue-cell tumors. A neuritic process, also called neuropil, is a pathognomonic feature of neuroblastoma cells. NSE, chromogranin, synaptophysin, and S-100 immunohistochemical stains are usually positive. More than 90% of patients have elevated urinary levels of homovanillic acid (HVA) and/or vanillylmandelic acid (VMA). The most important biologic marker is *MYCN (N-MYC)* of chromosome 2.

**Educational Objective:**

A cystic tumor in the cerebellum of a child is most likely a pilocytic astrocytoma. Biopsy will show a well-differentiated neoplasm comprised of spindle cells with hair-like glial processes that are associated with microcysts. These cells are mixed with Rosenthal fibers and granular eosinophilic bodies.



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www.ncbi.nlm.nih.gov/pubmed/11385046

A 42-year-old woman is brought to the office in summer due to 2 weeks of personality changes. Her family reports that she has become withdrawn and does not talk as much as before. She has also had difficulty picking things up with her right hand. The patient has HIV infection and does not take her antiretroviral therapy consistently. She is a former smoker and used injection drugs in the past. The patient works in a food-processing facility and has not traveled recently. Temperature is 37 C (98.6 F), blood pressure is 126/78 mm Hg, pulse is 82/min, and respirations are 14/min. The patient is oriented to time, place, and person but is slow to respond to questions. Motor strength is decreased in her right upper extremity, with an exaggerated biceps reflex. CD4 count is 78 cells/mm$^3$, and plasma HIV RNA (viral load) is 400,000 copies/mL. CT scan of the head shows a small hypodense area in the left frontal lobe with ring enhancement after intravenous contrast administration. Two similar lesions are present in the basal ganglia and cerebellum. Which of the following is the most likely route of transmission of the infectious agent causing this patient's current condition?

A. Bite from an insect

B. Close contact with an infected person

C. Ingestion of contaminated particles



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www.ncbi.nlm.nih.gov/pubmed/11385046

120/78 mm Hg, pulse is 82/min, and respirations are 14/min. The patient is oriented to time, place, and person but is slow to respond to questions. Motor strength is decreased in her right upper extremity, with an exaggerated biceps reflex. CD4 count is 78 cells/mm$^3$, and plasma HIV RNA (viral load) is 400,000 copies/mL. CT scan of the head shows a small hypodense area in the left frontal lobe with ring enhancement after intravenous contrast administration. Two similar lesions are present in the basal ganglia and cerebellum. Which of the following is the most likely route of transmission of the infectious agent causing this patient's current condition?

- A. Bite from an insect
- B. Close contact with an infected person
- C. Ingestion of contaminated particles
- D. Inhalation of bird droppings
- E. Scratch from an infected animal
- F. Unprotected sexual intercourse

Submit



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www.ncbi.nlm.nih.gov/pubmed/11385046

120/78 mm Hg, pulse is 82/min, and respirations are 14/min. The patient is oriented to time, place, and person but is slow to respond to questions. Motor strength is decreased in her right upper extremity, with an exaggerated biceps reflex. CD4 count is 78 cells/mm$^3$, and plasma HIV RNA (viral load) is 400,000 copies/mL. CT scan of the head shows a small hypodense area in the left frontal lobe with ring enhancement after intravenous contrast administration. Two similar lesions are present in the basal ganglia and cerebellum. Which of the following is the most likely route of transmission of the infectious agent causing this patient's current condition?

A. Bite from an insect (1%)

B. ~~Close contact with an infected person~~ (5%)

✓ C. Ingestion of contaminated particles (67%)

D. ~~Inhalation of bird droppings~~ (12%)

E. ~~Scratch from an infected animal~~ (12%)

F. ~~Unprotected sexual intercourse~~ (2%)



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| ***Toxoplasma* encephalitis** | |
|---|---|
| **Setting** | • Exposure to cat feces with subsequent ingestion of ***Toxoplasma gondii***<br>• Reactivation in setting of immunosuppression<br>• Primarily **AIDS** with **CD4 count <100/mm$^3$** |
| **Clinical** | • Headache<br>• Confusion<br>• Fever<br>• Focal neurologic deficits/seizures |
| **Diagnostic** | • Positive *Toxoplasma gondii* IgG<br>• Multiple **ring-enhancing** brain lesions |
| **Therapeutic** | • Sulfadiazine & pyrimethamine (leucovorin)<br>• Antiretroviral initiation<br>• Prophylaxis: **TMP-SMX** (CD4 count <100/mm$^3$) |


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| | |
|---|---|
| | • Prophylaxis: **TMP-SMX** (CD4 count <100/mm³) |

**TMP-SMX** = trimethoprim-sulfamethoxazole.

This patient with untreated AIDS has neurologic manifestations and multiple ring-enhancing brain lesions, raising strong suspicion for **toxoplasmic encephalitis**. The underlying pathogen is *Toxoplasma gondii*, an obligate intracellular parasite whose definitive host is **cats**. Transmission primarily occurs when individuals are exposed to contaminated **cat feces** (eg, litter box or cat handling) and subsequently **ingest oocytes**; it may also be transmitted by the consumption of undercooked meat from an intermediate host (eg, pig, sheep).

Healthy individuals rapidly contain the infection via a cell mediated immune response and rarely develop clinical symptoms. However, latent infection is established (tissue cysts), and reactivation can occur in the setting of immunocompromisation (eg, **advanced AIDS**). The most common manifestation of reactivation is toxoplasmic encephalitis, which is characterized by progressive headache, confusion, focal neurologic deficits, and/or seizure. Brain imaging classically shows multiple ring-enhancing lesions.

**(Choice A)** Mosquito bites can transmit viral pathogens (eg, West Nile, Zika) that can cause encephalitis. Patients may present with slowly worsening headache, confusion, seizure, or focal neurologic findings. However, viral pathogens do not typically cause ring-enhancing brain lesions.


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• Prophylaxis: TMP-SMX (CD4 count <100/mm³)

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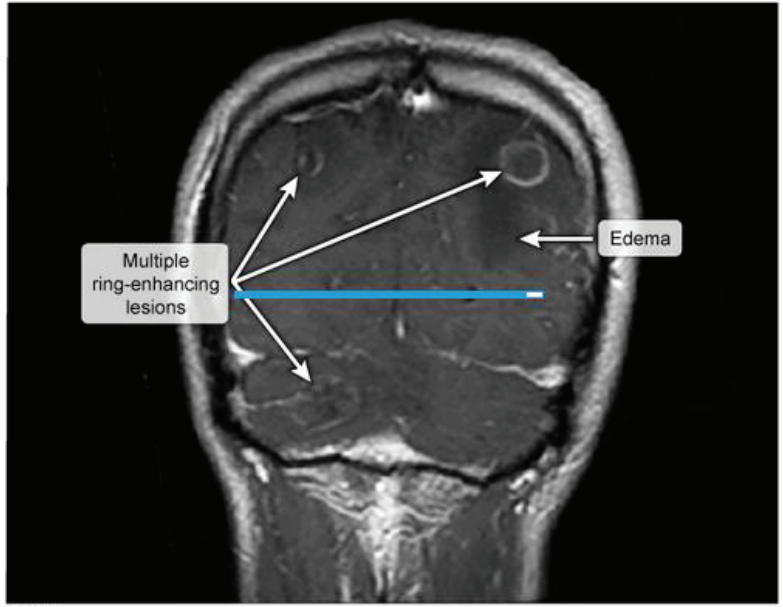
**Toxoplasma encephalitis**

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However, viral pathogens do not typically cause ring-enhancing brain lesions.

**(Choice B)** Herpes virus type 1 is typically transmitted by close contact (eg, kissing) with an infected patient who has active lesions. Although this virus is the most common cause of sporadic encephalitis, imaging usually shows inflammation in the temporal lobe with edema and mass effect.

**(Choice D)** *Cryptococcus neoformans*, a fungus found in soil contaminated by bird (especially pigeon) droppings, is a common cause of meningoencephalitis in patients with untreated AIDS and usually presents with slowly worsening fever, malaise, and headache. Brain imaging rarely shows lesions, but signs of elevated intracranial pressure (eg, hydrocephalus) may be present.

**(Choice E)** *Bartonella henselae* is a gram-negative bacterium transmitted to humans during a cat scratch. Healthy individuals can subsequently develop cat-scratch disease (regional lymphadenopathy), but patients with advanced AIDS are at risk for the more serious clinical syndrome of bacillary angiomatosis (violaceous, highly vascular skin lesions with constitutional symptoms). However, central nervous system manifestations are uncommon.

**(Choice F)** Syphilis can be transmitted by unprotected sexual intercourse, and patients with HIV are at greater risk for developing neurosyphilis. This often presents with confusion, meningeal symptoms (eg, stiff neck), eye abnormalities, and cranial nerve palsies. However, MRI of the brain usually shows leptomeningeal enhancement, not ring-enhancing lesions.



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However, viral pathogens do not typically cause ring-enhancing brain lesions.

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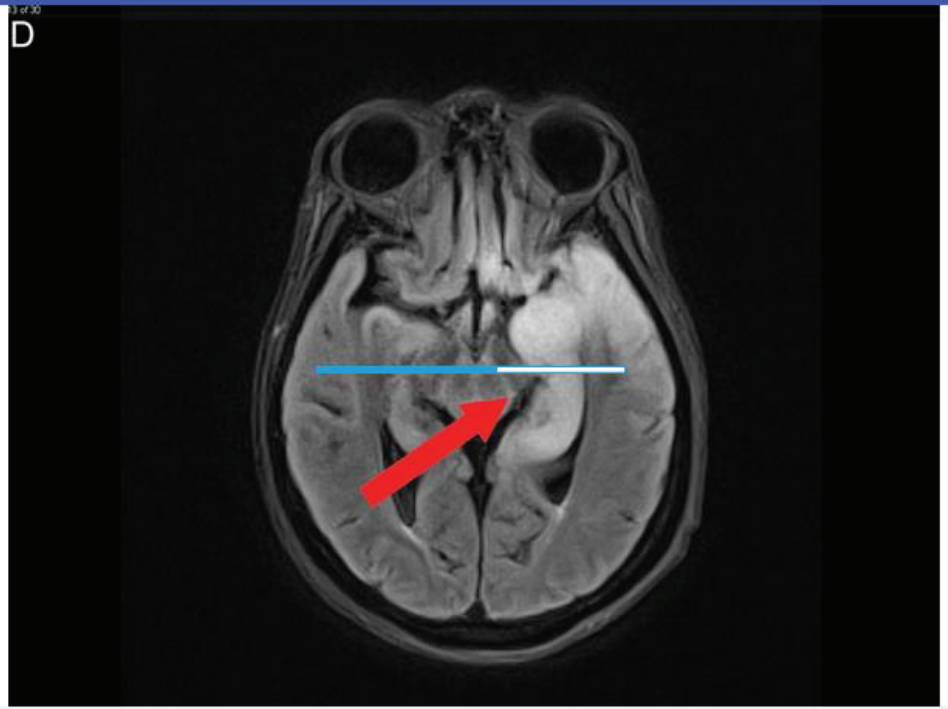


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with advanced AIDS are at risk for the more serious clinical syndrome of bacillary angiomatosis (violaceous, highly vascular skin lesions with constitutional symptoms). However, central nervous system manifestations are uncommon.

**(Choice F)** Syphilis can be transmitted by unprotected sexual intercourse, and patients with HIV are at greater risk for developing neurosyphilis. This often presents with confusion, meningeal symptoms (eg, stiff neck), eye abnormalities, and cranial nerve palsies. However, MRI of the brain usually shows leptomeningeal enhancement, not ring-enhancing lesions.

**Educational objective:**

*Toxoplasma gondii* is an intracellular parasite that is typically transmitted to humans after accidental ingestion of contaminated cat feces (eg, cat handling, litter box). Most initial cases are asymptomatic. However, the organism establishes a latent infection that can reactivate in the setting of severe immunocompromise, particularly advanced AIDS. Patients usually develop encephalitis with multiple ring-enhancing lesions.

| Microbiology | Nervous System | Toxoplasmosis |
|---|---|---|
| Subject | System | Topic |

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A 35-year-old man comes to the office due to a painful tongue sore. For the past 2 weeks he has had a fever and has experienced myalgias and arthralgias. He has no known medical problems. The patient works as a driver for a local delivery service. He had unprotected sex with a stranger approximately 1 month ago. Physical examination shows a rash over his trunk and cervical lymphadenopathy. An ulcer is located on the median sulcus of the tongue and is 2 cm anterior to the foramen cecum. Blood is drawn for an HIV test. The pain sensation from his ulcer is most likely carried by which of the following nerves?

A. Chorda tympani
B. Glossopharyngeal nerve
C. Mandibular division of the trigeminal nerve
D. Maxillary division of the trigeminal nerve
E. Vagus nerve

Submit



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A 35-year-old man comes to the office due to a painful tongue sore. For the past 2 weeks he has had a fever and has experienced myalgias and arthralgias. He has no known medical problems. The patient works as a driver for a local delivery service. He had unprotected sex with a stranger approximately 1 month ago. Physical examination shows a rash over his trunk and cervical lymphadenopathy. An ulcer is located on the median sulcus of the tongue and is 2 cm anterior to the foramen cecum. Blood is drawn for an HIV test. The pain sensation from his ulcer is most likely carried by which of the following nerves?

A. Chorda tympani (9%)
B. ~~Glossopharyngeal nerve~~ (27%)
C. Mandibular division of the trigeminal nerve (50%)
D. ~~Maxillary division of the trigeminal nerve~~ (8%)
E. ~~Vagus nerve~~ (3%)

Correct

50% Answered correctly
44 secs Time Spent
02/14/2021 Last Updated



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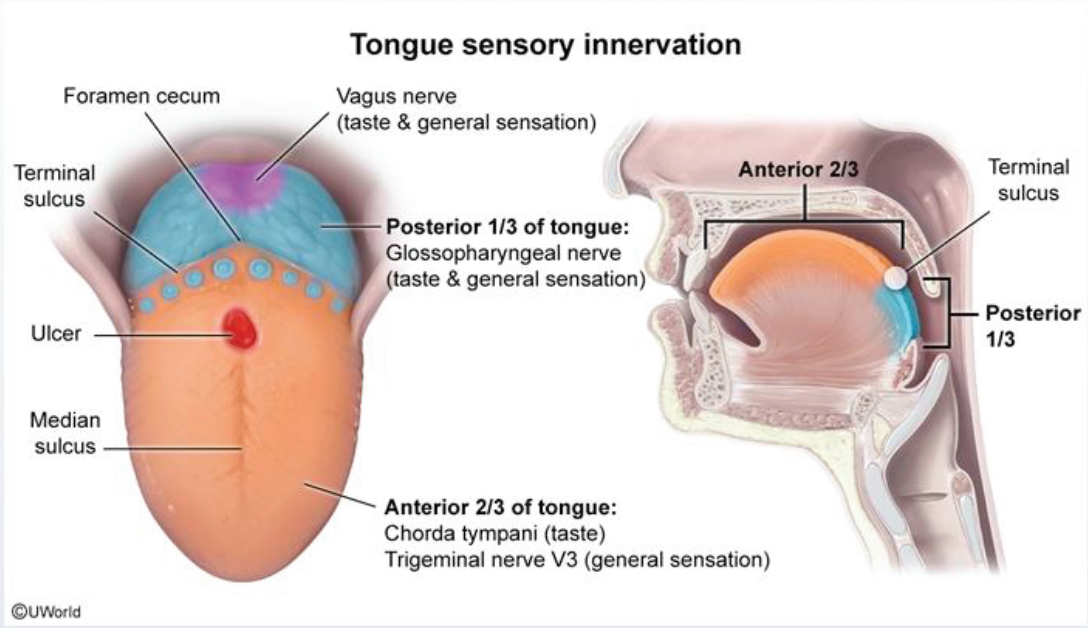


Acute HIV can present with rash, lymphadenopathy, fever, and painful oral ulcers on the tongue. Innervation of the tongue is complex, as there are motor, general sensory, and gustatory (taste) components.

1. **Motor innervation** of the tongue is provided by the hypoglossal nerve (cranial nerve [CN] XII) with the


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1. **Motor innervation** of the tongue is provided by the hypoglossal nerve (cranial nerve [CN] XII) with the exception of the palatoglossus muscle, which is innervated by the vagus nerve (CN X).
2. **General sensory** innervation of the tongue (including touch, pain, pressure, and temperature sensation) is provided by:
    - Anterior 2/3 of the tongue: mandibular branch of trigeminal nerve (CN $V_3$)
    - Posterior 1/3 of the tongue: glossopharyngeal nerve (CN IX)
    - Posterior area of the tongue root: vagus nerve (CN X)
3. **Gustatory innervation** (taste buds) is as follows:
    - Anterior 2/3 of the tongue: chorda tympani branch of facial nerve (CN VII)
    - Posterior 1/3 of the tongue: glossopharyngeal nerve (CN IX)
    - Posterior area of the tongue root and taste buds of the larynx and upper esophagus: vagus nerve (CN X)

Any lesion anterior to the terminal sulcus and foramen cecum, including this patient's oral ulcer, would be located on the **anterior** 2/3 of the tongue. **Pain** from this region (as well as sensations of touch, pressure, and temperature) is transmitted by the **mandibular branch of the trigeminal nerve**.

**(Choices A, B, and E)** The chorda tympani branch of the facial nerve (CN VII) transmits gustatory sensation from the anterior 2/3 of the tongue but not painful stimuli. The glossopharyngeal nerve (CN IX)


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and temperature) is transmitted by the **mandibular branch of the trigeminal nerve**.

**(Choices A, B, and E)** The chorda tympani branch of the facial nerve (CN VII) transmits gustatory sensation from the anterior 2/3 of the tongue but not painful stimuli. The glossopharyngeal nerve (CN IX) transmits taste, pain, temperature, and touch stimuli from the posterior 1/3 of the tongue. The vagus nerve (CN X) innervates the far posterior area of the tongue root, transmitting both gustatory and general sensory stimuli.

**(Choice D)** The maxillary division of the trigeminal nerve (CN $V_2$) does not participate in tongue innervation.

**Educational objective:**
General sensation from the anterior 2/3 of the tongue is carried by the mandibular division of the trigeminal nerve. Gustatory innervation of the anterior 2/3 of the tongue is provided by the chorda tympani branch of the facial nerve.

| Anatomy | Nervous System | Trigeminal nerve |
|---|---|---|
| Subject | System | Topic |

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A 21-year old man is brought to the emergency department due to head trauma sustained during a boxing match. During the fight, he had a brief loss of consciousness after a hard hit to the right side of his face. He has a headache and muffled hearing in his right ear. On examination, the patient is alert and oriented. Palpation of the head does not reveal any step-offs. Cervical spine examination is normal. Otoscopic examination reveals hemotympanum in the right ear. This patient is at greatest risk for injury involving which of the following cranial nerves?

- A. Olfactory nerve
- B. Oculomotor nerve
- C. Trigeminal nerve
- D. Facial nerve
- E. Hypoglossal nerve

Submit



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A. Olfactory nerve (0%)
B. Oculomotor nerve (1%)
C. Trigeminal nerve (14%)
D. Facial nerve (82%)
E. Hypoglossal nerve (1%)

Correct

82% Answered correctly

42 secs Time Spent

11/24/2020 Last Updated



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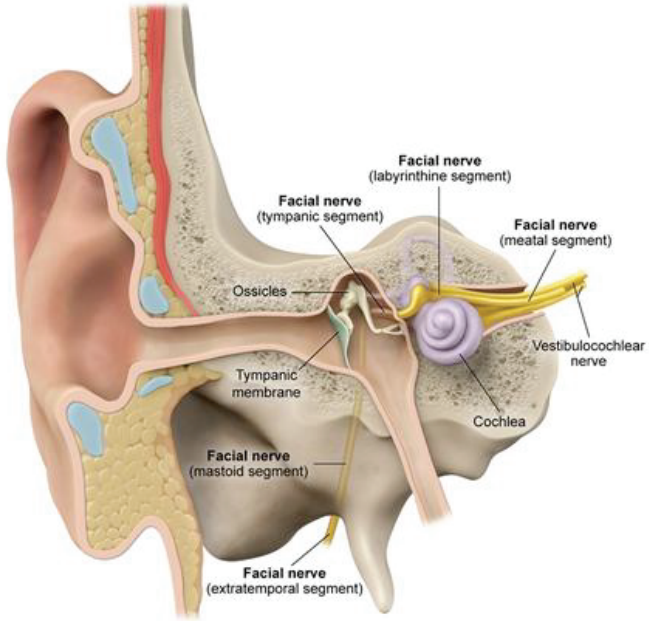
Exhibit Display

Facial nerve course through the temporal bone

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(mastoid segment)



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This patient who sustained trauma to the head now has hearing loss and **hemotympanum**, which is concerning for a **temporal bone fracture**. Contained within the temporal bone are many structures involved in hearing, including the external auditory canal, tympanic membrane, ossicular chain, cochlea, and vestibulocochlear nerve (CN VIII). Injury or disruption to any of these structures can cause **hearing loss**, as in this patient.

The temporal bone also contains the **facial nerve (CN VII)**, which originates in the brainstem and then enters the temporal bone at the internal auditory meatus. It **travels** through the internal auditory canal with the vestibulocochlear nerve (CN VIII) and then takes a complicated route **through the temporal bone** itself, traveling near the otic capsule, through the middle ear, and then through the mastoid portion to exit at the stylomastoid foramen.

Because of its location, the facial nerve is at risk of injury in temporal bone fractures. Deficits can be diverse and significant because the facial nerve has many functions, including:

- Movement of the face, including eye closure
- Taste from the anterior 2/3 of the tongue
- Parasympathetic innervation of submandibular and lacrimal glands
- Sound dampening (due to innervation of the stapedius muscle)



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- Taste from the anterior 2/3 of the tongue
- Parasympathetic innervation of submandibular and lacrimal glands
- Sound dampening (due to innervation of the stapedius muscle)

**(Choice A)** Axons of chemoreceptor cells make up the olfactory nerve (CN I) rootlets, which project through the cribriform plate of the ethmoid bone. Acceleration-deceleration head injuries can lead to avulsion of the olfactory nerve rootlets, but this would not be associated with hearing loss or hemotympanum.

**(Choice B)** The oculomotor nerve (CN III) exits the skull base from the superior orbital fissure and is at risk with trauma to the orbit or anterior face.

**(Choice C)** The trigeminal nerve (CN V) divides into V1, V2, and V3, which exit the skull base from the superior orbital fissure, foramen rotundum, and foramen ovale, respectively, which are all located in the sphenoid bone. These branches are at risk with trauma to the orbit or anterior face.

**(Choice E)** The hypoglossal nerve (CN XII) exits the skull base through the hypoglossal canal of the occipital bone. It could be injured by fractures involving the occipital bone, but it is more commonly injured due to penetrating neck trauma.

**Educational objective:**



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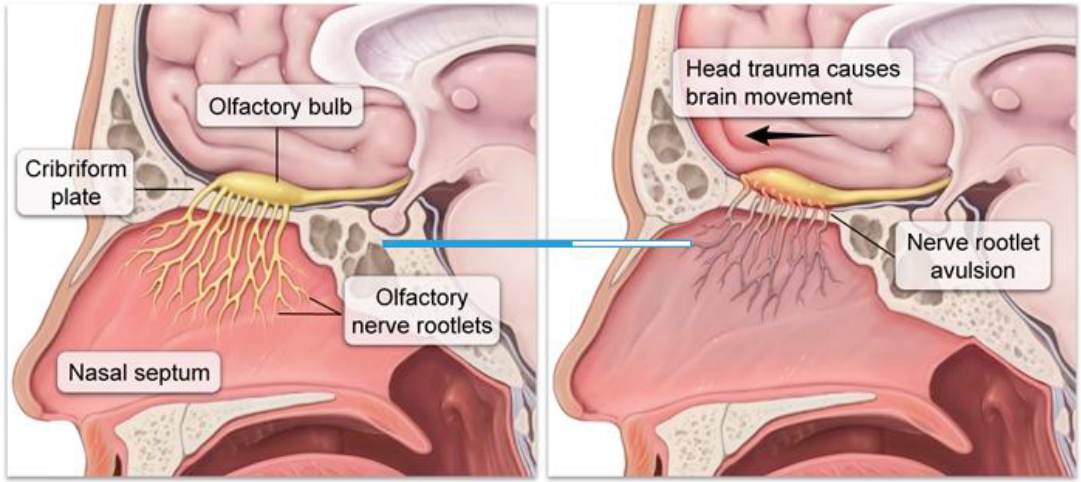
## Olfactory nerve rootlet avulsion with TBI




**TBI** = traumatic brain injury.

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Educational objective:



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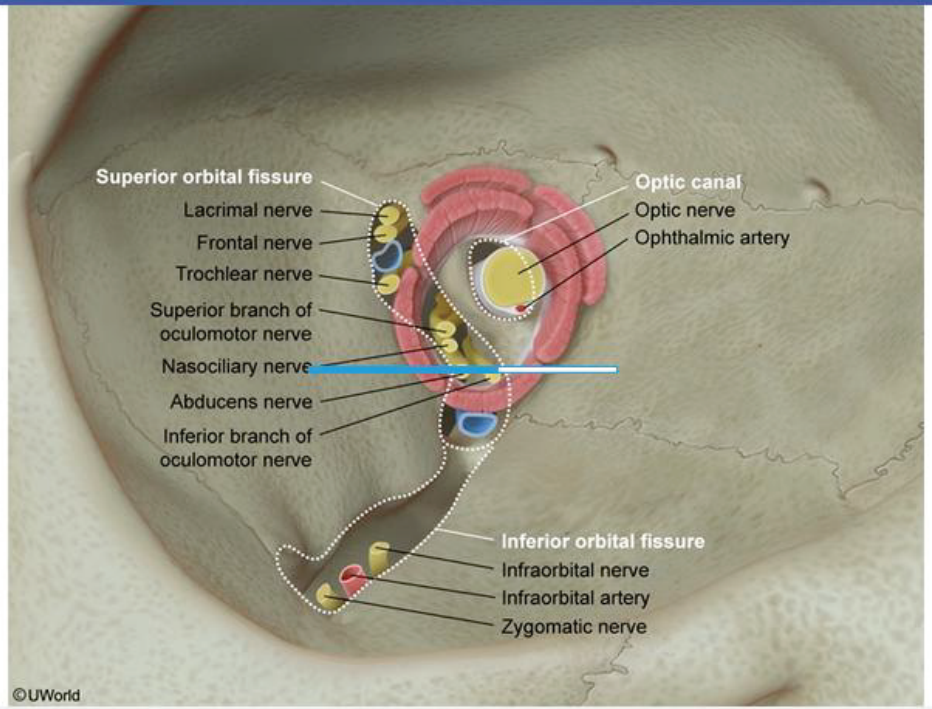


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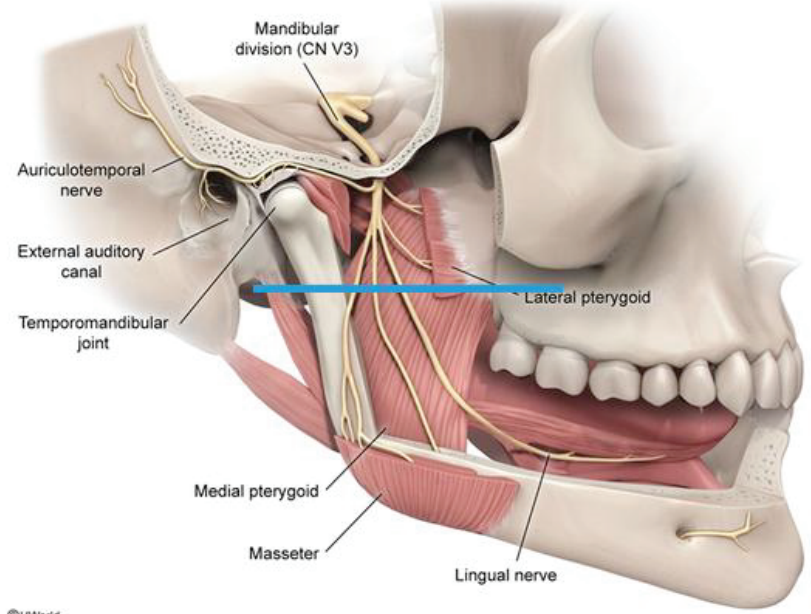
Mandibular division of trigeminal nerve

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Educational objective:



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**(Choice B)** The oculomotor nerve (CN III) exits the skull base from the superior orbital fissure and is at risk with trauma to the orbit or anterior face.

**(Choice C)** The trigeminal nerve (CN V) divides into V1, V2, and V3, which exit the skull base from the superior orbital fissure, foramen rotundum, and foramen ovale, respectively, which are all located in the sphenoid bone. These branches are at risk with trauma to the orbit or anterior face.

**(Choice E)** The hypoglossal nerve (CN XII) exits the skull base through the hypoglossal canal of the occipital bone. It could be injured by fractures involving the occipital bone, but it is more commonly injured due to penetrating neck trauma.

**Educational objective:**

In addition to much of the hearing apparatus (eg, ossicles, cochlea, vestibulocochlear nerve), the temporal bone also contains the facial nerve, which can be injured in temporal bone fractures.

**References**

- Facial Nerve Anatomy and Clinical Applications

| Anatomy | Nervous System | Skull fractures |
|---|---|---|
| Subject | System | Topic |

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A 24-year-old man comes to the emergency department after injuring his shoulder. He was standing on a ladder hanging pictures in his living room when he lost his balance and fell, impacting his left shoulder on the hardwood floor. Radiographs show an anterior dislocation of the humerus. Reduction of the patient's dislocated joint is performed under procedural sedation with intravenous propofol. A single bolus of propofol provides adequate sedation for the procedure, and he becomes clinically alert several minutes after administration. Which of the following mechanisms most likely explains this patient's rapid recovery from anesthesia?

A. Liver elimination of the drug
B. Lung elimination of the drug
C. Renal elimination of the drug
D. Spontaneous degradation in plasma
E. Tissue redistribution of the drug

Submit



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A. Liver elimination of the drug (12%)
B. Lung elimination of the drug (8%)
C. Renal elimination of the drug (6%)
D. Spontaneous degradation in plasma (9%)
E. Tissue redistribution of the drug (64%)

64%  01 min, 04 secs  10/24/2020


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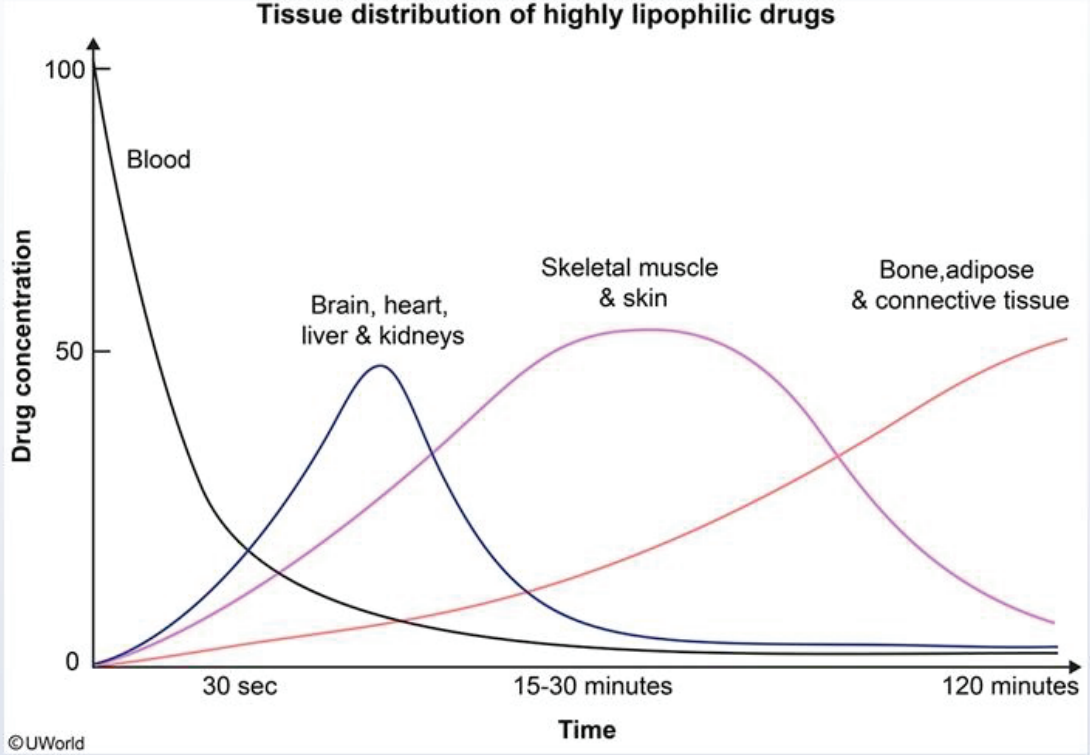


**Propofol** is a highly lipophilic anesthetic drug used for both induction and maintenance of general



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**Propofol** is a highly lipophilic anesthetic drug used for both induction and maintenance of general anesthesia as well as procedural sedation. When administered as an intravenous bolus, its onset of action is approximately 30 seconds with a duration of action typically lasting <10 minutes. Administration causes a rapid decrease in the level of consciousness as well as a global amnestic effect.

Following bolus infusion, propofol is rapidly cleared from the plasma and **preferentially distributed** to organs receiving **high blood flow** (eg, brain). This initial distribution accounts for the rapid onset of sedation seen with its administration. Over time, propofol is **redistributed** to organs receiving less blood flow (eg, fat, muscle tissue). Because the site of action for propofol is the brain, redistribution accounts for the rapid termination of drug action.

**(Choice A)** Although propofol is metabolized in the liver through hepatic conjugation, its half-life is 4 hours to 1 day; therefore, hepatic metabolism does not occur fast enough to account for such a short duration of action.

**(Choice B)** Volatile, inhaled anesthetics such as halothane are predominately eliminated by the lungs.

**(Choice C)** Renal tubular secretion and glomerular filtration are the predominate mechanisms through which water-soluble drugs are eliminated.

**(Choice D)** Atracurium is a non-depolarizing neuromuscular blocking agent that spontaneously degrades


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to 1 day; therefore, hepatic metabolism does not occur fast enough to account for such a short duration of action.

**(Choice B)** Volatile, inhaled anesthetics such as halothane are predominately eliminated by the lungs.

**(Choice C)** Renal tubular secretion and glomerular filtration are the predominate mechanisms through which water-soluble drugs are eliminated.

**(Choice D)** Atracurium is a non-depolarizing neuromuscular blocking agent that spontaneously degrades in plasma and organ tissue, a type of metabolism known as Hofmann elimination.

**Educational objective**

Propofol and other highly lipophilic drugs readily diffuse across membranes, quickly accumulating in tissues receiving high blood flow; this accounts for their rapid onset of action. These compounds are subsequently redistributed to organs receiving less blood flow, which explains their short duration of action.

**References**

- Propofol. A review of its pharmacodynamic and pharmacokinetic properties and use as an intravenous anesthetic



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A 32-year-old man comes to the emergency department due to a 2-day history of progressive difficulty walking and tingling in his feet. He says that his feet feel "like they've gone to sleep" and states that he tripped while walking this morning. Medical history is unremarkable except for an episode of acute diarrhea 2 weeks ago that resolved spontaneously. The patient takes no medications. He drinks 1-2 alcoholic beverages daily and does not use tobacco products or illicit drugs. Vital signs are within normal limits. Physical examination shows decreased muscular strength in the lower extremities bilaterally with absent deep tendon reflexes. Which of the following agents is most likely associated with this patient's condition?

- A. *Campylobacter jejuni*
- B. Rotavirus
- C. *Salmonella*
- D. Shiga toxin–producing *Escherichia coli*
- E. *Shigella*
- F. Zika virus


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walking and tingling in his feet. He says that his feet feel "like they've gone to sleep" and states that he tripped while walking this morning. Medical history is unremarkable except for an episode of acute diarrhea 2 weeks ago that resolved spontaneously. The patient takes no medications. He drinks 1-2 alcoholic beverages daily and does not use tobacco products or illicit drugs. Vital signs are within normal limits. Physical examination shows decreased muscular strength in the lower extremities bilaterally with absent deep tendon reflexes. Which of the following agents is most likely associated with this patient's condition?

- ✓ A. *Campylobacter jejuni* (93%)
- B. Rotavirus (1%)
- C. *Salmonella* (0%)
- D. Shiga toxin–producing *Escherichia coli* (1%)
- E. *Shigella* (1%)
- F. Zika virus (1%)

Correct

93%

32 secs

03/12/2021



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| Guillain-Barré syndrome | |
|---|---|
| **Mechanism** | • Immune-mediated polyneuropathy due to cross-reacting antibodies (molecular mimicry) |
| **Triggering events** | • *Campylobacter jejuni*<br>• Viral illness (eg, HIV, upper respiratory viral illness)<br>• Trauma/surgery<br>• Vaccinations |
| **Pathology** | • Endoneurial inflammation<br>• Segmental demyelination & axon damage |
| **Manifestations** | • Symmetric, progressive muscle weakness<br>• Depressed deep tendon reflexes<br>• Paresthesias; back pain<br>• Respiratory compromise |

This patient with progressive lower extremity weakness, depressed deep tendon reflexes, and paresthesias has **Guillain-Barré syndrome** (GBS). GBS represents a group of immune-mediated demyelinating


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| | |
|---|---|
| | • Respiratory compromise |

This patient with progressive lower extremity weakness, depressed deep tendon reflexes, and paresthesias has **Guillain-Barré syndrome** (GBS). GBS represents a group of immune-mediated demyelinating polyneuropathies that are thought to be caused by **molecular mimicry**. An antecedent event (typically an infection) provokes an immune response that cross-reacts with the Schwann cells and myelin sheath of the peripheral nerves. The myelin sheath is stripped from the axon, leading to loss of neuronal conductivity and axonal degeneration. Up to one-third of GBS cases are preceded by ***Campylobacter jejuni*** infection, a common cause of acute (sometimes bloody) **diarrhea**. Less common antecedent infections include upper respiratory viral illnesses, Epstein-Barr virus, cytomegalovirus, Zika virus, and HIV.

Patients with GBS experience **symmetric**, **ascending weakness** that typically begins in the legs and progresses to flaccid paralysis and respiratory failure. Decreased or absent deep tendon reflexes, paresthesias, pain (often of the back), and dysautonomia are common.

**(Choices B, C, D, and E)** Rotavirus, *Salmonella*, Shiga toxin–producing *Escherichia coli*, and *Shigella* are all important causes of diarrhea but are not associated with GBS. Both Shiga toxin–producing *E coli* and *Shigella* can cause bloody diarrhea and are associated with hemolytic uremic syndrome. Salmonella typically causes nonbloody diarrhea and may lead to bacteremia, particularly in an asplenic patient.


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all important causes of diarrhea but are not associated with GBS. Both Shiga toxin–producing *E coli* and *Shigella* can cause bloody diarrhea and are associated with hemolytic uremic syndrome. Salmonella typically causes nonbloody diarrhea and may lead to bacteremia, particularly in an asplenic patient. Rotavirus, most commonly seen in children, causes nonbloody diarrhea and can lead to gastrointestinal obstruction due to small bowel intussusception.

**(Choice F)** Zika virus is associated with GBS; however, patients with Zika virus typically present with a pruritic maculopapular rash, low-grade fever, arthralgias, and conjunctivitis rather than diarrhea.

**Educational objective:**
Guillain-Barré syndrome represents a group of immune-mediated polyneuropathies that are thought to be caused by molecular mimicry, leading to demyelination of the peripheral nerves. Up to one-third of GBS cases are preceded by a *Campylobacter jejuni* infection, which is a common cause of acute diarrheal illness.

| Microbiology | Nervous System | Guillain Barre syndrome |
|---|---|---|
| Subject | System | Topic |

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A 10-year-old boy whose family recently immigrated to the United States is brought to the physician with ataxia, myoclonus, and visual problems. His parents say that he began acting strangely and having difficulty with school work several months ago. After the appropriate workup, a brain biopsy is obtained and an RNA virus containing hemagglutinin is cultured from the tissue sample. Which of the following is the most likely diagnosis?

A. Creutzfeldt-Jakob disease
B. Guillain-Barré syndrome
C. Multiple sclerosis
D. Progressive multifocal leukoencephalopathy
E. Progressive supranuclear palsy
F. Subacute sclerosing panencephalitis

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A 10-year-old boy whose family recently immigrated to the United States is brought to the physician with ataxia, myoclonus, and visual problems. His parents say that he began acting strangely and having difficulty with school work several months ago. After the appropriate workup, a brain biopsy is obtained and an RNA virus containing hemagglutinin is cultured from the tissue sample. Which of the following is the most likely diagnosis?

A. Creutzfeldt-Jakob disease (6%)
B. ~~Guillain-Barré syndrome~~ (4%)
C. ~~Multiple sclerosis~~ (1%)
D. Progressive multifocal leukoencephalopathy (21%)
E. ~~Progressive supranuclear palsy~~ (3%)
F. Subacute sclerosing panencephalitis (63%)

Correct

63%
Answered correctly

01 min, 54 secs
Time Spent

10/02/2020
Last Updated



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| Measles virus (rubeola) | |
|---|---|
| **Clinical presentation** | • Prodrome (eg, cough, coryza, conjunctivitis, fever, Koplik spots)<br>• Maculopapular exanthem<br>  ○ Cephalocaudal & centrifugal spread<br>  ○ Spares palms/soles |
| **Complications** | • Primary measles pneumonia<br>• Secondary bacterial infections (pneumonia & otitis media)<br>• Neurologic<br>  ○ Encephalitis (within days)<br>  ○ Acute disseminated encephalomyelitis (within weeks)<br>  ○ Subacute sclerosing panencephalitis (within years) |
| **Prevention** | • Live attenuated measles vaccine |

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**Measles virus** is an enveloped, single-stranded RNA virus that is a member of the paramyxovirus family. Its genome codes for several viral structural proteins, including membrane-bound **hemagglutinin** (mediates cell surface adhesion) and **matrix protein** (important for viral assembly).

**Subacute sclerosing panencephalitis (SSPE)** is a rare complication of measles that occurs in children or



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(mediates cell surface adhesion) and **matrix protein** (important for viral assembly).

**Subacute sclerosing panencephalitis (SSPE)** is a rare complication of measles that occurs in children or young adults several years after the initial infection. It is thought to be caused by a form of measles virus with a mutated or **absent matrix protein** that prevents mature (enveloped) virion particles from forming. However, the virus continues to replicate intracellularly, leading to a persistent, nonproductive infection that evades eradication by the immune system. **Accumulation of viral nucleocapsids** within neurons and oligodendrocytes results in the formation of intranuclear inclusions and eventually leads to inflammation, demyelination, and gliosis in many cerebral areas.

Patients with SSPE have high titers of **measles antibodies** in the serum and cerebrospinal fluid (detectable as oligoclonal bands). The disease causes various neurologic deficits and dementia, and is relentlessly progressive and fatal.

**(Choice A)** Creutzfeldt-Jakob disease is a rare form of rapidly progressive dementia that is caused by prions (abnormally folded proteins). It usually occurs in older patients (sporadic form), although younger patients can be affected after consuming prion-infected meat products (acquired or variant form). Brain biopsy will show spongiform transformation of the cerebral cortex.

**(Choice B)** Guillain-Barré syndrome is a postinfectious autoimmune demyelinating disorder of the


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**(Choice B)** Guillain-Barré syndrome is a postinfectious autoimmune demyelinating disorder of the peripheral nervous system. It most commonly presents as a symmetrical ascending weakness with absent reflexes following an infectious respiratory or diarrheal illness.

**(Choice C)** Multiple sclerosis usually manifests in patients 20-30 years old. It is characterized by a variety of visual (eg, optic neuritis, internuclear ophthalmoplegia) and sensory deficits occurring in a relapsing/remitting pattern. Brain biopsy will show focal demyelinated plaques with relative axonal sparing.

**(Choice D)** Progressive multifocal leukoencephalopathy is an infectious demyelinating disorder caused by JC virus, a double-stranded DNA virus in the polyomavirus family. JC virus manifests with progressive neurologic deficits in immunocompromised individuals (eg, lymphoma, leukemia, or HIV infection).

**(Choice E)** Progressive supranuclear palsy is a form of parkinsonism resulting from neurodegeneration of the midbrain and frontal subcortical white matter. It presents with rapidly progressive gait dysfunction and falls, executive function loss, and vertical gaze palsy. Brain biopsy usually shows deposits of abnormally phosphorylated tau proteins.

**Educational objective:**
Subacute sclerosing panencephalitis is a rare complication of measles infection that occurs several years after apparent recovery from initial infection. Oligoclonal bands of measles virus antibodies are found in


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of visual (eg, optic neuritis, internuclear ophthalmoplegia) and sensory deficits occurring in a relapsing/remitting pattern. Brain biopsy will show focal demyelinated plaques with relative axonal sparing.

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**Educational objective:**
Subacute sclerosing panencephalitis is a rare complication of measles infection that occurs several years after apparent recovery from initial infection. Oligoclonal bands of measles virus antibodies are found in the cerebrospinal fluid of these patients.

**References**

- Subacute sclerosing panencephalitis: clinical and demographic characteristics.



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A 45-year-old quadriplegic man with suspected bacterial pneumonia is admitted to the hospital and started on intravenous antibiotics. Over the next 24 hours, he develops progressive respiratory failure requiring mechanical ventilation. Prior to intubation, a skeletal muscle relaxant is administered and the patient subsequently goes into cardiac arrest. His attached cardiac monitor shows ventricular fibrillation. While he is being resuscitated, his serum potassium level is drawn and later comes back as 9.5 mEq/L. Administration of which of the following agents is most likely responsible for this patient's condition?

A. Atracurium
B. Baclofen
C. Dantrolene
D. Succinylcholine
E. Vecuronium

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A. Atracurium (5%)
B. Baclofen (7%)
C. Dantrolene (10%)
D. Succinylcholine (70%)
E. Vecuronium (6%)

Correct

70%
Answered correctly

53 secs
Time Spent

02/28/2021
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**Adverse effects of succinylcholine**

- Malignant hyperthermia (especially with halothane) in genetically susceptible patients
- Severe hyperkalemia in patients with burns, myopathies, crush injuries, and denervation
- Bradycardia from parasympathetic stimulation or tachycardia from sympathetic effects

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Succinylcholine is a depolarizing neuromuscular-blocking agent that, like acetylcholine, attaches to the nicotinic acetylcholine receptor (nAChR) and depolarizes the neuromuscular end plate. Unlike acetylcholine, succinylcholine is not degraded by acetylcholinesterase, resulting in continuous stimulation of the endplate (reflected by initial transient fasciculations). However, the sodium channels surrounding the end plate rapidly become inactivated and cannot reopen until the end plate is repolarized. Thus, succinylcholine-induced depolarization remains isolated to the end plate, resulting in development of a flaccid paralysis (**phase 1 block**). Eventually, with continued administration of succinylcholine, the continuous depolarization of the endplate gives way to gradual repolarization as the nAChR becomes desensitized to the effects of succinylcholine. This is termed **phase II block** and is similar to non-



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depolarizing blockade.

Because the nAChR is a nonselective cation channel, its opening not only allows sodium influx but also potassium release. Exaggerated hyperkalemia and life-threatening arrhythmias can occur in patients with crush or burn injuries, denervating injuries or diseases (eg, quadriplegia and Guillain-Barré syndrome), and myopathies. These pathologic states cause up-regulation of muscle nAChRs and/or rhabdomyolysis, which can result in the release of large amounts of potassium when succinylcholine is administered. In these patients, non-depolarizing agents such as vecuronium or rocuronium are better choices (**Choice E**).

**(Choice A)** The nondepolarizing neuromuscular-blocking agent atracurium releases histamine and can produce a fall in blood pressure, flushing, and bronchoconstriction. It is also metabolized to laudanosine, which can provoke seizures.

**(Choice B)** Baclofen is a muscle relaxant that affects $GABA_B$ receptors at the level of the spinal cord.

**(Choice C)** Dantrolene is a muscle relaxant effective in malignant hyperthermia. It acts on ryanodine receptors on the sarcoplasmic reticulum and prevents release of calcium into the cytoplasm of muscle fibers.

**Educational objective:**


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**(Choice C)** Dantrolene is a muscle relaxant effective in malignant hyperthermia. It acts on ryanodine receptors on the sarcoplasmic reticulum and prevents release of calcium into the cytoplasm of muscle fibers.

**Educational objective:**
Succinylcholine can cause significant potassium release and life-threatening arrhythmias in patients at high risk for hyperkalemia, including those with burns, myopathies, crush injuries, and denervating injuries or disease.

**References**

- Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms.


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A 57-year-old man comes to the office accompanied by his wife for follow-up of Parkinson disease. The patient reports no change in motor symptoms, and the disease has been well controlled with anti-Parkinson medication. However, his wife is very concerned about a change in behavior, reporting that he recently started gambling and has lost a significant amount of their savings. The patient drives several hours multiple times a week to gamble at a casino in a neighboring state. His only other medical condition is major depressive disorder for which he takes sertraline. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination shows a mild resting hand tremor and minimal rigidity. Which of the following is most likely responsible for this patient's recent change in behavior?

A. Decreased peripheral conversion of levodopa
B. Increased norepinephrine levels in synaptic cleft
C. Increased serotonin levels in synaptic cleft
D. Stimulation of central dopamine receptors
E. Upregulation of brain nicotinic acetylcholine receptors


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A. Decreased peripheral conversion of levodopa (7%)
B. Increased norepinephrine levels in synaptic cleft (3%)
C. Increased serotonin levels in synaptic cleft (21%)
D. Stimulation of central dopamine receptors (63%)
E. Upregulation of brain nicotinic acetylcholine receptors (3%)

Correct

63%

01 min, 35 secs

01/20/2021



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Parkinson disease (PD) is caused by loss of dopaminergic neurons in the basal ganglia, resulting in symptoms of bradykinesia, tremor, and rigidity. Dopaminergic medications used to treat PD have been associated with the abrupt onset of **impulse control disorders**, including **pathological gambling**, compulsive buying, and compulsive sexual behavior. **Dopamine agonists** (eg, pramipexole) as a class are most frequently associated with this adverse effect. These drugs act by binding to central dopamine receptors and stimulating dopamine activity in the ventral striatum (includes the **nucleus accumbens**, which is involved in motivation and **reward pathways**) and substantia nigra.

Patients on dopamine agonist therapy should be monitored for dysfunctional impulse control. Gradual taper of the offending agent results in improvement in most cases.

**(Choice A)** Decreased peripheral conversion of levodopa is the mechanism of action of carbidopa, a drug used in combination with levodopa (a dopamine precursor) to increase the availability of levodopa in the central nervous system. Compared to dopamine agonists, carbidopa-levodopa is much less likely to precipitate impulse control disorders.

**(Choice B)** Increasing norepinephrine levels in the synaptic cleft is the mechanism of action of atomoxetine, a nonstimulant medication used in the treatment of attention deficit hyperactivity disorder.

**(Choice C)** Increasing serotonin levels in the synaptic cleft is the mechanism of action of selective


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central nervous system. Compared to dopamine agonists, carbidopa-levodopa is much less likely to precipitate impulse control disorders.

**(Choice B)** Increasing norepinephrine levels in the synaptic cleft is the mechanism of action of atomoxetine, a nonstimulant medication used in the treatment of attention deficit hyperactivity disorder.

**(Choice C)** Increasing serotonin levels in the synaptic cleft is the mechanism of action of selective serotonin reuptake inhibitors (eg, sertraline). These medications are not associated with the onset of impulse control disorders and have actually been shown to decrease impulsivity.

**(Choice E)** Upregulation of brain nicotinic acetylcholine receptors is a neuroadaptive response to the receptor desensitization that occurs with chronic repeated exposure to high levels of nicotine.

**Educational objective:**

Dopamine agonist medications used to treat Parkinson disease have been associated with the abrupt onset of impulse control disorders, including pathological gambling, compulsive buying, and compulsive sexual behavior. The behavior is thought to be mediated by stimulation of central dopamine receptors.

**References**

- Dopamine agonists and impulse control disorders: a complex association.



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A 64-year-old man comes to the office with 2 months of episodic facial pain. He describes sudden-onset, severe, electric shock-like pain over the right cheek and ear lasting several seconds. The patient reports that activities like shaving and washing his face can trigger the pain and it is becoming more frequent. He is a retired veteran and has a history of posttraumatic stress disorder. Physical examination, including neurologic examination, is normal. Laboratory studies for blood cell counts, electrolytes, and hepatic and renal function are normal. The patient is started on a single drug therapy. On a follow-up visit 3 months later, he reports symptom improvement but is found to have the following blood counts:

| | |
|---|---|
| Hemoglobin | 9.0 g/dL |
| Reticulocytes | 0.1% |
| Platelets | 80,000/mm$^3$ |
| Leukocytes | 2,500/mm$^3$ |

Which of the following is the most likely mechanism of action of the drug used in this patient?

A. Blocks NMDA receptors in hippocampal neurons



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|---|---|
| Hemoglobin | 9.0 g/dL |
| Reticulocytes | 0.1% |
| Platelets | 80,000/mm$^3$ |
| Leukocytes | 2,500/mm$^3$ |

Which of the following is the most likely mechanism of action of the drug used in this patient?

A. Blocks NMDA receptors in hippocampal neurons
B. Blocks serotonin reuptake on multiple levels
C. Decreases calcium current in thalamic neurons
D. Decreases sodium current on multiple levels
E. Increases chloride current on multiple levels
F. Inhibits synaptic acetylcholinesterase in cortical neurons

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| | |
|---|---|
| Reticulocytes | 0.1% |
| Platelets | 80,000/mm$^3$ |
| Leukocytes | 2,500/mm$^3$ |

Which of the following is the most likely mechanism of action of the drug used in this patient?

A. Blocks NMDA receptors in hippocampal neurons (6%)
B. Blocks serotonin reuptake on multiple levels (9%)
C. Decreases calcium current in thalamic neurons (8%)
D. Decreases sodium current on multiple levels (66%)
E. Increases chloride current on multiple levels (7%)
F. Inhibits synaptic acetylcholinesterase in cortical neurons (1%)

Correct

66%
Answered correctly

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Time Spent

11/09/2020
Last Updated



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This patient has **trigeminal neuralgia** (tic douloureux), a neuropathic disorder that typically presents with episodic, severe, unilateral, electric shock-like pain in the distribution of CN V. Symptoms are often triggered by innocuous stimuli such as shaving or washing the face. The first-line treatment of trigeminal neuralgia is **carbamazepine**, a neuroleptic medication that inhibits neuronal high-frequency firing by reducing the ability of **sodium channels** to recover from inactivation.

Carbamazepine may cause the following important adverse effects:

1. **Bone marrow suppression**, which may lead to anemia, agranulocytosis, and thrombocytopenia (complete blood cell counts should be monitored periodically)
2. Syndrome of inappropriate antidiuretic hormone secretion leading to hyponatremia

**(Choice A)** Ketamine, felbamate, and memantine are examples of medications that block NMDA receptors. Ketamine is used as a general anesthetic agent, felbamate is an anticonvulsant, and memantine may be effective in the treatment of Alzheimer dementia.

**(Choice B)** Selective serotonin reuptake inhibitors (eg, fluoxetine, sertraline) are typically used to treat depression, anxiety, and posttraumatic stress disorder. Side effects may include headache, worsening anxiety/agitation, and insomnia.


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depression, anxiety, and posttraumatic stress disorder. Side effects may include headache, worsening anxiety/agitation, and insomnia.

**(Choice C)** Ethosuximide blocks T-type $Ca^{2+}$ channels and decreases calcium current in thalamic neurons. This anticonvulsant is the agent of choice for absence seizures. Major side effects include gastrointestinal symptoms and drowsiness.

**(Choice E)** Various antiseizure medications (eg, benzodiazepines, barbiturates) act on the GABA-A receptor to increase chloride conductance; however, carbamazepine does not significantly affect chloride channels.

**(Choice F)** Donepezil is an acetylcholinesterase inhibitor that can be used to treat Alzheimer dementia. Side effects are generally related to increased cholinergic activity, which includes gastrointestinal symptoms and symptomatic bradycardia.

**Educational objective:**
The first-line treatment for trigeminal neuralgia is carbamazepine, a neuroleptic medication that inhibits neuronal high-frequency firing by reducing the ability of sodium channels to recover from inactivation. Carbamazepine can cause bone marrow suppression; therefore, complete blood cell counts should be monitored periodically.


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A 23-year-old man is brought to the emergency department after sustaining stab injuries in a street fight. The patient feels lightheaded and dizzy. His blood pressure is 100/60 mm Hg and pulse is 115/min. Physical examination shows profuse bleeding from penetrating wounds over the left neck and shoulder area. Intravenous fluids are administered, and a blood transfusion is initiated. Urgent surgical exploration is performed, and the injured blood vessel is repaired. Further exploration shows complete transection of the nerve indicated by the arrow in the image below.

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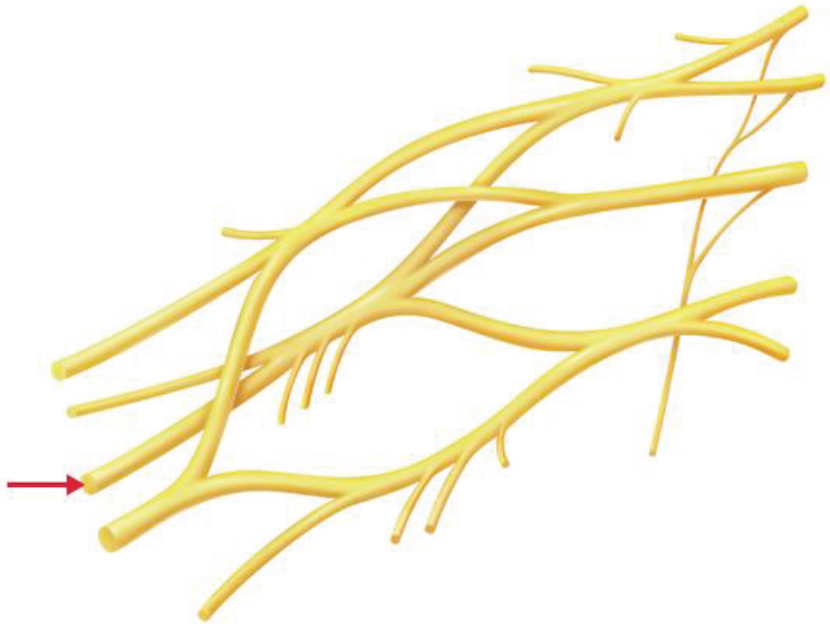

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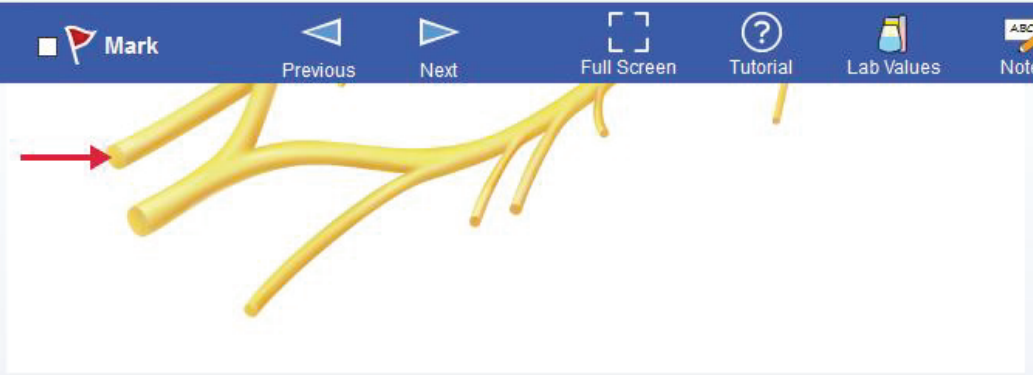

Which of the following actions is most likely to be weakened as a result of this patient's nerve injury?

A. Abduction of the fingers
B. Adduction of the thumb
C. Extension of the wrist
D. Flexion of the wrist
E. Opposition of the thumb

Submit



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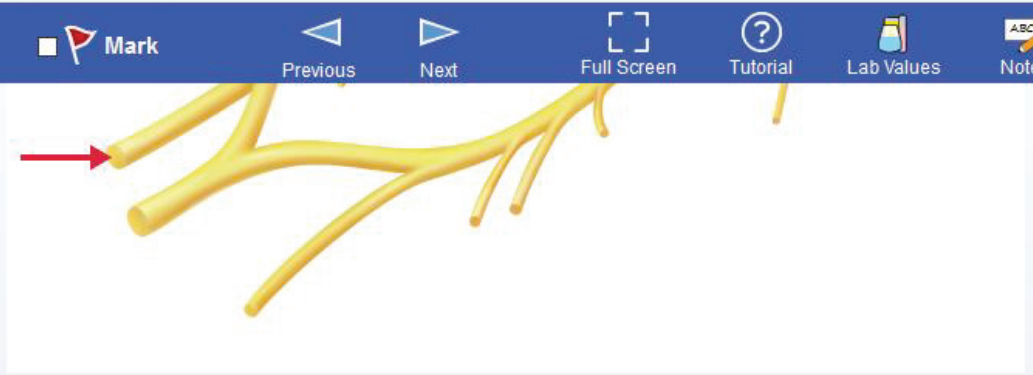

Which of the following actions is most likely to be weakened as a result of this patient's nerve injury?

A. ~~Abduction of the fingers~~ (3%)

B. ~~Adduction of the thumb~~ (3%)

✓ C. Extension of the wrist (76%)

D. ~~Flexion of the wrist~~ (10%)

E. Opposition of the thumb (5%)

Correct

76%

42 secs

11/17/2020



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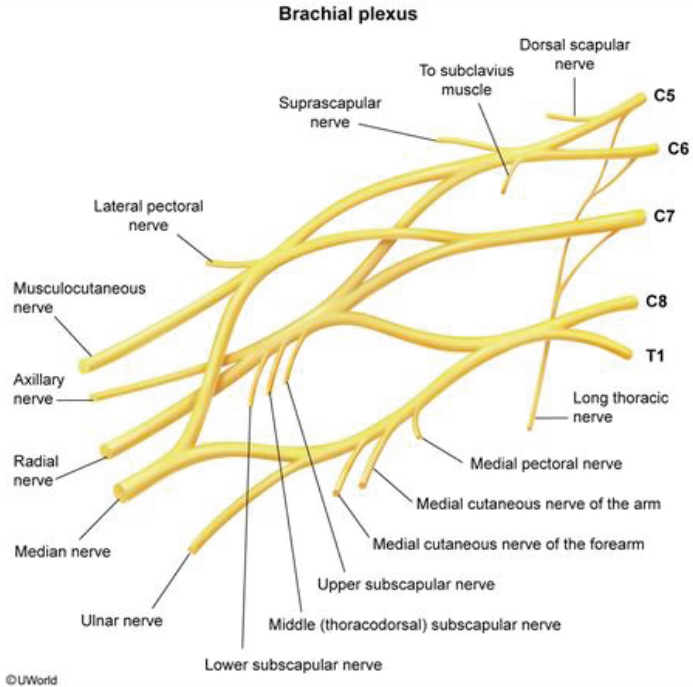


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The radial nerve is the largest branch of the brachial plexus and receives fibers from C5-T1. It innervates all of the extensor muscles of the upper limb below the shoulder and provides sensory innervation to the skin of the posterior arm, forearm, and dorsal lateral hand.

This nerve tracks within the radial groove on the humerus; therefore, it is vulnerable to traumatic injury (eg, penetrating stab wound) at the **humeral midshaft**. The nerve can also be injured during its superficial course within the **axilla**. Patients with proximal radial neuropathy typically have weakness during wrist and finger extension (wrist drop) and variable sensory loss over the posterior arm and forearm.

**(Choices A, B, D, and E)** Damage to the median or ulnar nerve can result in weakness on wrist flexion. Damage to the median nerve can also result in weakness on thumb opposition, whereas ulnar nerve damage may limit finger abduction and thumb adduction.

**Educational objective:**
The radial nerve provides sensory innervation to the skin of the posterior arm, forearm, and dorsal lateral hand and provides motor innervation to all of the extensor muscles of the upper limb below the shoulder. Damage to the proximal radial nerve (eg, at the axilla or midshaft humerus) may result in wrist drop.

**References**

- Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical



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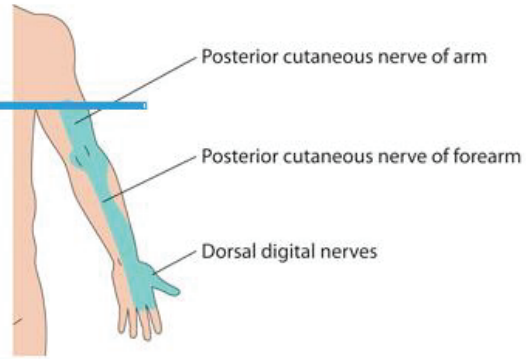
Exhibit Display

## Important nerves in the arm

| Nerve | Motor function | Region of sensory loss with neuropathy |
|---|---|---|
| Radial nerve | Extension at all arm, wrist, & finger joints below the shoulder, forearm supination, thumb abduction in plane of palm | |

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• Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical



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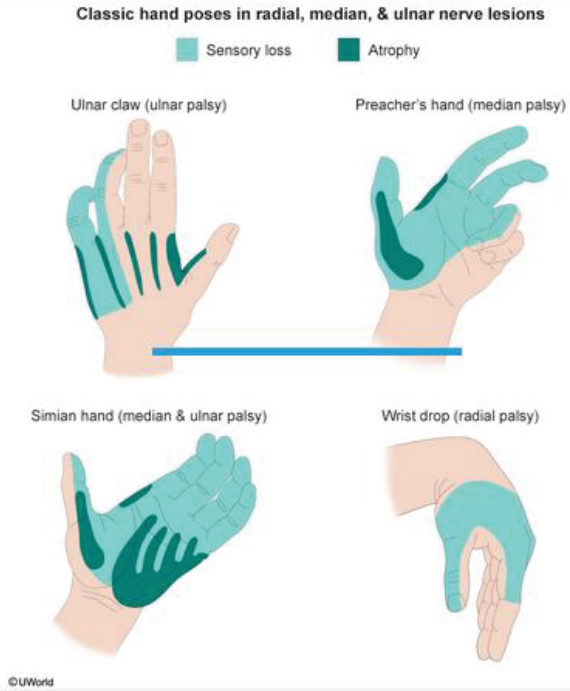


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- Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical



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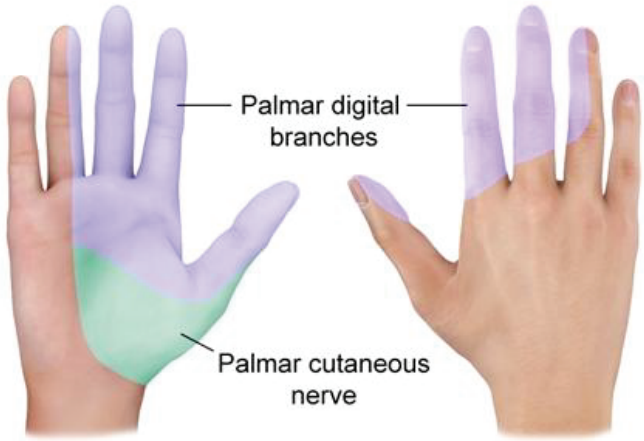
Exhibit Display

## Median nerve

| Motor function | Cutaneous innervation |
|---|---|
| • Thumb flexion & opposition<br>• Flexion of digits 2 & 3<br>• Wrist flexion & abduction<br>• Forearm pronation |  |



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• Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical



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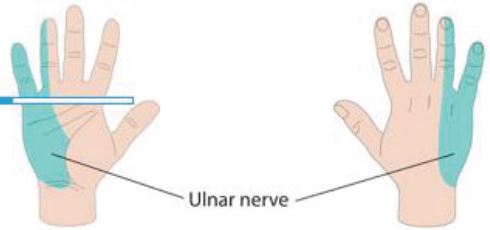
## Exhibit Display

| Nerve | Motor function | Region of sensory loss with neuropathy |
|---|---|---|
| Ulnar nerve | Finger abduction & adduction other than thumb, thumb adduction, flexion of digits 4 & 5, wrist flexion & adduction |  |



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- Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical



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The radial nerve is the largest branch of the brachial plexus and receives fibers from C5-T1. It innervates all of the extensor muscles of the upper limb below the shoulder and provides sensory innervation to the skin of the posterior arm, forearm, and dorsal lateral hand.

This nerve tracks within the radial groove on the humerus; therefore, it is vulnerable to traumatic injury (eg, penetrating stab wound) at the **humeral midshaft**. The nerve can also be injured during its superficial course within the **axilla**. Patients with proximal radial neuropathy typically have weakness during wrist and finger extension (wrist drop) and variable sensory loss over the posterior arm and forearm.

**(Choices A, B, D, and E)** Damage to the median or ulnar nerve can result in weakness on wrist flexion. Damage to the median nerve can also result in weakness on thumb opposition, whereas ulnar nerve damage may limit finger abduction and thumb adduction.

**Educational objective:**

The radial nerve provides sensory innervation to the skin of the posterior arm, forearm, and dorsal lateral hand and provides motor innervation to all of the extensor muscles of the upper limb below the shoulder. Damage to the proximal radial nerve (eg, at the axilla or midshaft humerus) may result in wrist drop.

**References**

- Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical



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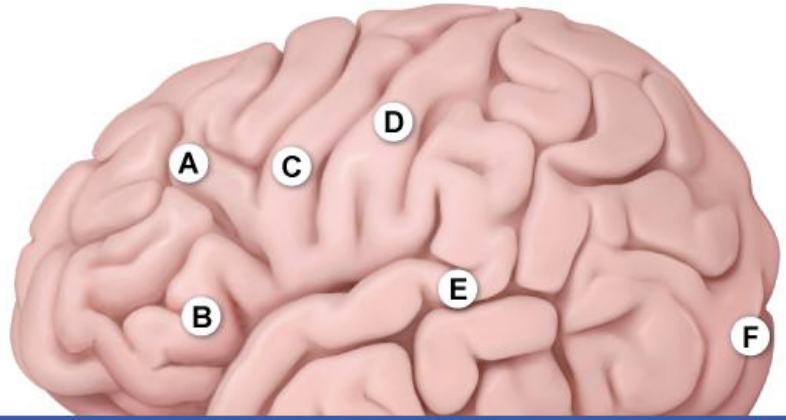
A 54-year-old man is brought to the emergency department by his wife after he develops difficulty speaking. When asked about the onset of his symptoms, the patient slowly responds with "I... weak... morning..." and becomes very frustrated. His wife says that he was able to grasp a pen without any problem while completing medical release forms, but had trouble signing his name. On examination, he is able to state his first name but with difficulty, and correctly points to different body parts on command. He also has mild weakness involving his right arm and face. This patient's speech difficulties are most likely caused by a lesion affecting which of the following brain areas?



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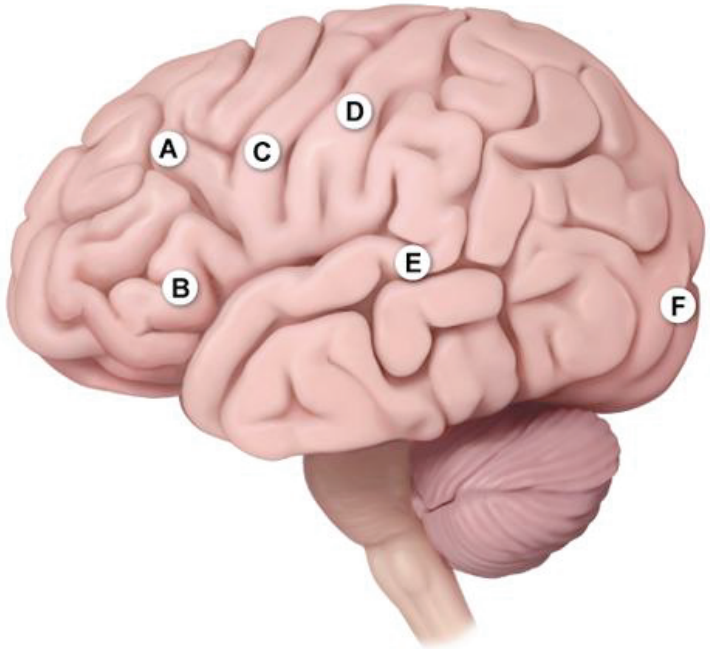


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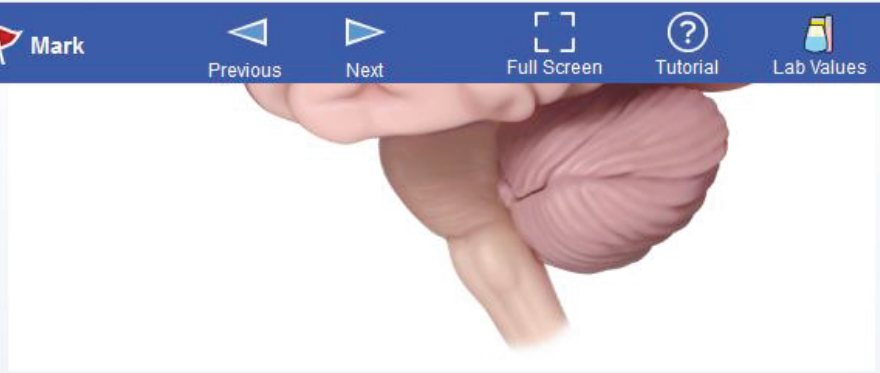

- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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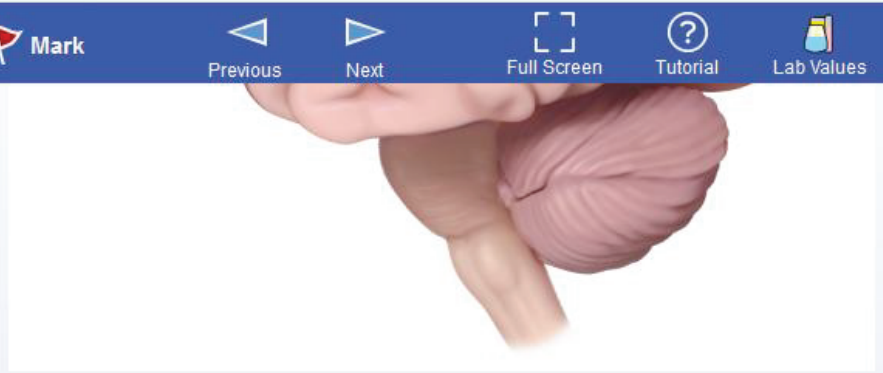

A. A (1%)
B. B (72%)
C. C (14%)
D. D (2%)
E. E (9%)
F. F (0%)

Correct

72%

01 min, 56 secs

10/06/2020



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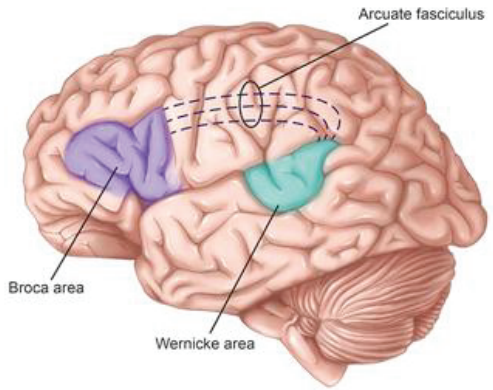
## Exhibit Display

### Common types of aphasia




| Aphasia syndrome | Spontaneous speech | Comprehension | Repetition | Associated features |
|---|---|---|---|---|
| Broca | Sparse & nonfluent | Relatively preserved | Impaired | Right hemiparesis (face & upper limb) |
| Wernicke | Fluent & voluminous but lacks meaning | Greatly diminished | Impaired | Right superior visual field defect |
| Conduction | Fluent with phonemic errors | Relatively preserved | Very poor | None |

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This patient most likely has **Broca (motor, nonfluent) aphasia**. This condition classically results from damage to Broca area of the brain, the region responsible for all communicative motor planning. Individuals are able to communicate meaningfully, but their speech is slow and consists primarily of nouns and verbs. Speech may be punctuated by pauses after each word as the patient attempts to verbalize the next. Patients also often have difficulty writing and signing, and become frustrated as they have insight into their expressive language difficulties. They can understand spoken language and follow commands (intact speech comprehension) as Wernicke area is unaffected.

Broca area is in the caudal part of the **inferior frontal gyrus** of the **dominant (usually left) hemisphere** (Brodmann areas 44 and 45). Patients may have associated **right hemiparesis** involving the upper limb and face due to this region's proximity to the primary motor cortex.

**(Choice A)** The frontal eye field is found near the caudal end of the middle frontal gyrus anterior to the precentral sulcus (Brodmann areas 6 and 8). Damage here would cause the eyes to deviate to the ipsilateral side.

**(Choice C)** Lesions to the precentral gyrus (primary motor cortex) can cause slurred speech (dysarthria) due to paresis/paralysis of the skeletal muscles involved in movements of the mouth, tongue, and larynx. Damage to Broca area is often associated with right-sided hemiparesis and oral apraxia due to extension of



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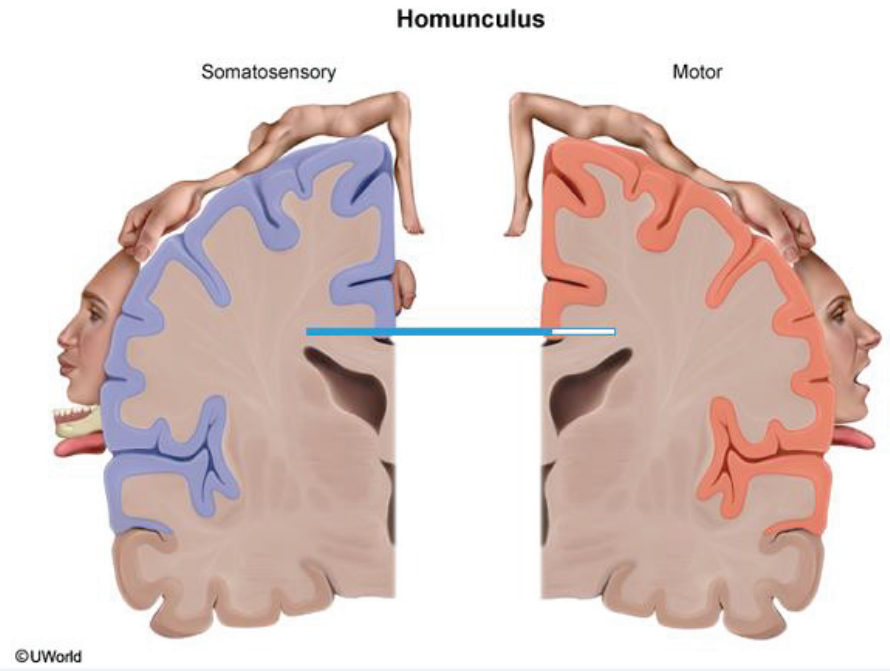


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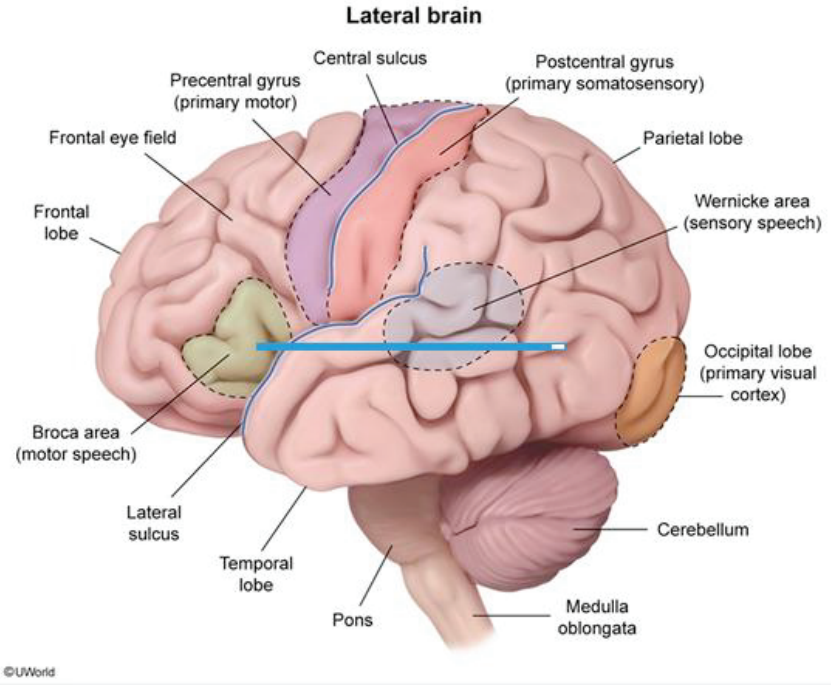


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Damage to Broca area is often associated with right-sided hemiparesis and oral apraxia due to extension of the lesion into the ipsilateral motor regions. However, it is injury to Broca area that leads to **language deficit**.

**(Choice D)** This is the postcentral gyrus (primary somatosensory cortex). A lesion here would cause sensation loss in the corresponding area of the contralateral body.

**(Choice E)** The caudal superior temporal gyrus (Brodmann area 22) is in the Wernicke area. A lesion here would cause a sensory (receptive) aphasia. Wernicke aphasia is also known as fluent aphasia in that speech flows readily but is meaningless ("word salad"). Patients typically lack insight into their problem.

**(Choice F)** A lesion to the visual cortex can cause cortical blindness or visual impairment that can make reading and writing difficult. Spoken speech would be unaffected.

**Educational objective:**
Broca (motor, nonfluent) aphasia results from damage to the inferior frontal gyrus of the dominant hemisphere. Patients are often frustrated as they understand language but cannot properly formulate the motor commands to write or form words (eg, slow, fragmented speech). Aphasia may be associated with right upper limb and face weakness due to extension of the lesion into the primary motor cortex.

**References**


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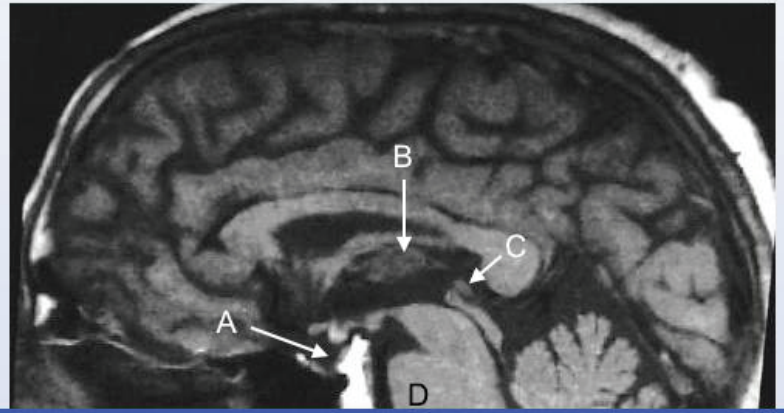
A 4-year-old boy is brought to the office due to headaches that have worsened progressively over the past month and are most severe when lying down. He also has had nonbloody, nonbilious emesis for 2 weeks that typically occurs early in the morning. In addition, the child has intermittent blurry vision, particularly when looking up at the mirror while brushing his teeth. Physical examination shows bilateral papilledema, inability to gaze upwards, and bilateral eyelid retraction. Laboratory testing of sodium, growth hormone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) is normal. Given the early morning emesis and papilledema, a brain mass is suspected and a brain MRI is ordered. Which of the following is the most likely location of the brain lesion in this patient?



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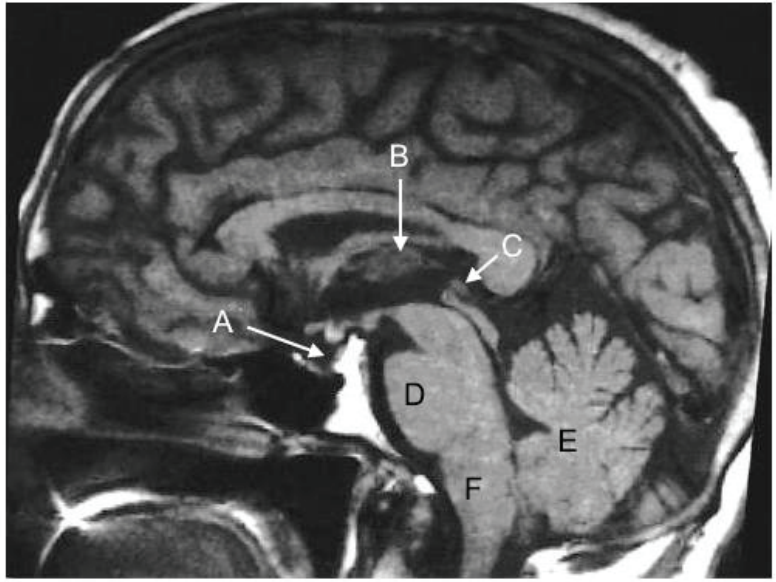


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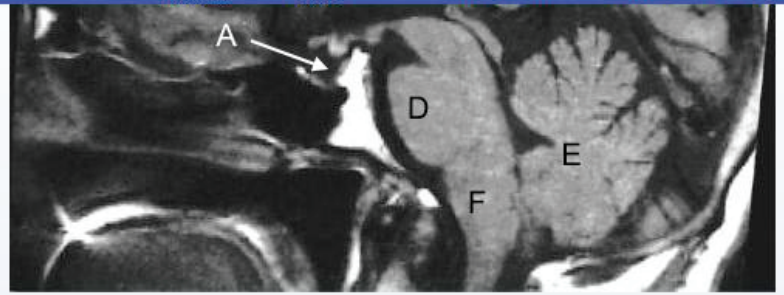


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- F. F

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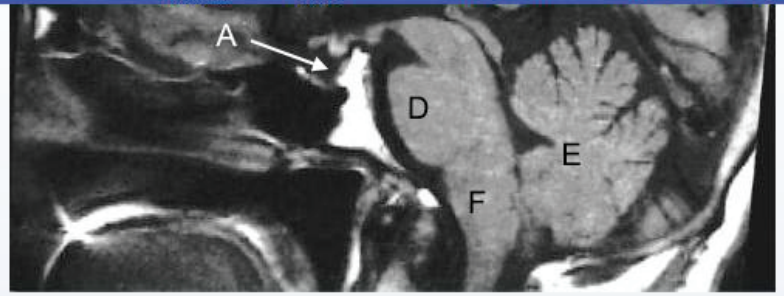


- A.A (20%)
- B.B (7%)
- ✓ C.C (41%)
- D.D (10%)
- E.E (9%)
- F. F (11%)

Correct

41%

01 min, 38 secs

03/05/2021



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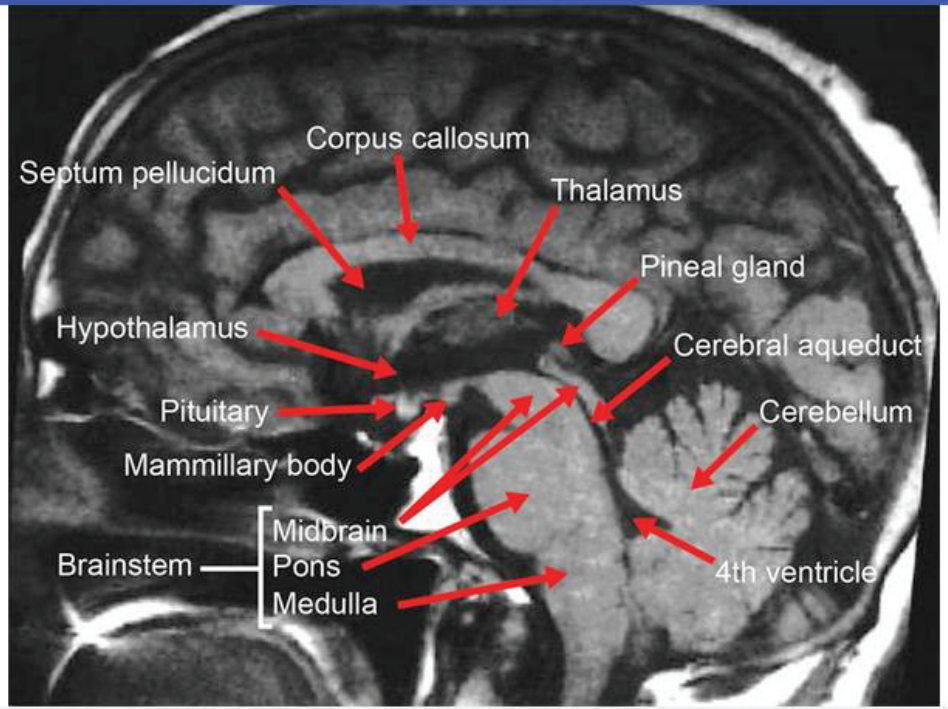


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This patient has a **pineal gland mass**. Classic manifestations of a pineal gland mass include **obstructive hydrocephalus** from aqueductal stenosis (papilledema, headache, and vomiting) and **dorsal midbrain (Parinaud) syndrome** due to direct compression of the pretectal region of the midbrain. Parinaud syndrome is characterized by limitation of upward gaze with a downward gaze preference, bilateral eyelid retraction (eg, Collier sign, sclera visible above the superior corneal limbus), and light-near dissociation (eg, pupils that react to accommodation but not to light). Diagnosis of pineal gland mass is made by brain MRI.

The most common pineal mass is a **germinoma**, a **midline** malignant tumor thought to arise from embryonic germ cells. A germinoma can also arise in the gonads or mediastinum and is more common in young boys. The most common locations for intracranial germinomas are the pineal gland and the suprasellar region (less common site) **(Choice A)**. Due to their proximity to the pituitary gland and hypothalamus, suprasellar germinomas do not lead to Parinaud syndrome, but they are more likely to present with endocrinopathies (eg, central precocious puberty, diabetes insipidus).

**(Choice B)** Primary thalamic tumors are rare. Damage to the thalamus from a mass or more commonly infarction/hemorrhage presents with contralateral hemisensory loss, behavioral changes, and language deficits.



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**(Choice D)** Pontine hemorrhage or tumor may cause "locked-in" syndrome, which is characterized by spastic quadriplegia and paralysis of most cranial nerves (CNs) with preserved consciousness and eye movements.

**(Choice E)** The most common cerebellar tumor in children is medulloblastoma, which typically presents with gait and limb ataxia, intention tremor, and nystagmus.

**(Choice F)** Lesions of the medulla can cause lateral and medial medullary syndromes. Lateral medullary (Wallenberg) syndrome leads to contralateral loss of pain and temperature sensations along with ipsilateral paralysis of CNs V, IX, X, and XI. Medial medullary syndrome causes contralateral spastic paralysis, contralateral sensory loss of vibration and proprioception, and ipsilateral flaccid paralysis of the tongue (CN XII).

**Educational objective:**
Germinomas are the most common pineal gland tumor and present with obstructive hydrocephalus and dorsal midbrain (Parinaud) syndrome. Germinomas in the suprasellar region cause endocrinopathies due to pituitary/hypothalamic dysfunction.

**References**

- Pineal germinoma.


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A 67-year-old woman with a known history of lung cancer comes to the office due to hoarseness and difficulty swallowing. She has no disturbances in vision or hearing. On examination, there is loss of the gag reflex on the left side; when the patient is prompted to say "ah," the uvula deviates to the right side. Her left shoulder is drooped and strength is reduced during left shoulder shrug testing. Chest x-ray shows a right lower lobe lung mass and several osteolytic rib lesions. MRI of the head also demonstrates multiple lesions consistent with metastasis. A lesion involving which of the following anatomical structures is most likely responsible for this patient's symptoms?

A. Cerebellopontine angle
B. Foramen magnum
C. Foramen ovale
D. Foramen rotundum
E. Hypoglossal canal
F. Jugular foramen



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difficulty swallowing. She has no disturbances in vision or hearing. On examination, there is loss of the gag reflex on the left side; when the patient is prompted to say "ah," the uvula deviates to the right side. Her left shoulder is drooped and strength is reduced during left shoulder shrug testing. Chest x-ray shows a right lower lobe lung mass and several osteolytic rib lesions. MRI of the head also demonstrates multiple lesions consistent with metastasis. A lesion involving which of the following anatomical structures is most likely responsible for this patient's symptoms?

A. ~~Cerebellopontine angle~~ (4%)
B. ~~Foramen magnum~~ (11%)
C. ~~Foramen ovale~~ (2%)
D. ~~Foramen rotundum~~ (2%)
E. Hypoglossal canal (8%)
✓ F. Jugular foramen (69%)

Correct
69%
02 mins, 17 secs
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Exhibit Display

| | Skull foramen | Traversing structures |
|---|---|---|
| **Anterior cranial fossa** | Cribriform plate | CN I olfactory bundles |
| **Middle cranial fossa** | Optic canal | CN II, ophthalmic artery, central retinal vein |
| | Superior orbital fissure | CN III, IV, $V_1$, VI, ophthalmic vein, sympathetic fibers |
| | Foramen rotundum | CN $V_2$ (maxillary) |
| | Foramen ovale | CN $V_3$ (mandibular) |
| | Foramen spinosum | Middle meningeal artery & vein |
| **Posterior cranial fossa** | Internal acoustic meatus | CN VII, VIII |
| | Jugular foramen | CN IX, X, XI, jugular vein |
| | Hypoglossal canal | CN XII |
| | Foramen magnum | Spinal roots of CN XI, brain stem, vertebral arteries |

CN = cranial nerve.

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Hypoglossal canal CN XII



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This patient's symptoms are consistent with a lesion involving the jugular foramen , a large aperture located in the base of the skull behind the carotid canal. It is formed by the petrous portion of the temporal bone and the occipital bone. Passing through the jugular foramen are cranial nerves (CN) IX, X, and XI. Lesions of the jugular foramen (eg, due to tumors, trauma, or infection) can result in **jugular foramen (Vernet) syndrome**, which is characterized by **CN IX**, **X**, and **XI dysfunction**. Symptoms are related to the nerve affected:

- Loss of taste from the posterior 1/3 of the tongue (CN IX)
- Loss of gag reflex (CN IX, X)
- Dysphagia (CN IX, X)
- Dysphonia/hoarseness (CN X)
- Soft palate drop with deviation of the uvula toward the normal side (CN X)
- Sternocleidomastoid and trapezius muscle paresis (CN XI)

**(Choice A)** Lesions at the cerebellopontine angle (eg, vestibular schwannoma) typically cause sensorineural hearing loss and tinnitus due to dysfunction of CN VIII.

**Educational objective:**



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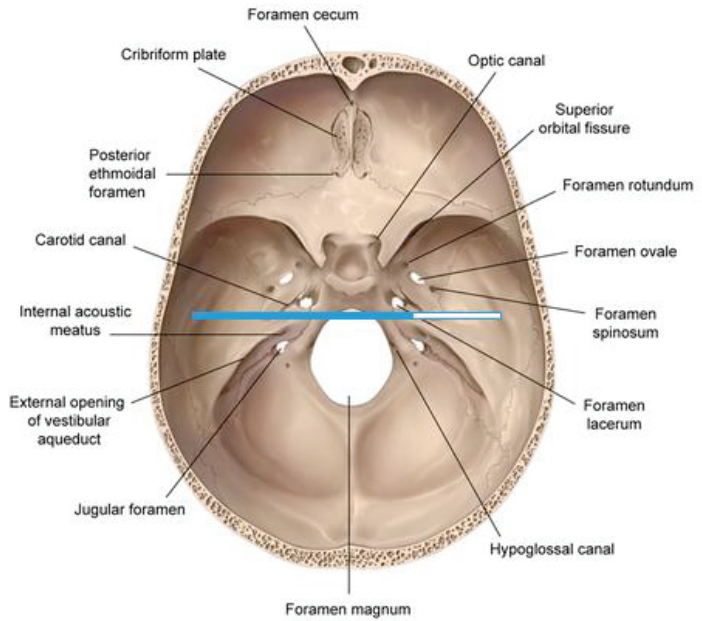
## Exhibit Display

### Foramina of the cranial base

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affected:

- Loss of taste from the posterior 1/3 of the tongue (CN IX)
- Loss of gag reflex (CN IX, X)
- Dysphagia (CN IX, X)
- Dysphonia/hoarseness (CN X)
- Soft palate drop with deviation of the uvula toward the normal side (CN X)
- Sternocleidomastoid and trapezius muscle paresis (CN XI)

**(Choice A)** Lesions at the cerebellopontine angle (eg, vestibular schwannoma) typically cause sensorineural hearing loss and tinnitus due to dysfunction of CN VIII.

**Educational objective:**

Lesions of the jugular foramen can result in jugular foramen (Vernet) syndrome, which is characterized by the dysfunction of cranial nerves IX, X, and XI. Symptoms include dysphagia, hoarseness, loss of gag reflex on the ipsilateral side, and deviation of the uvula toward the normal side.

**References**

- Jugular foramen syndrome as initial presentation of metastatic lung cancer.



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An intracranial mass is removed from a 33-year-old patient. The mass is composed of cells that have elongated, wavy nuclei. A biphasic pattern of growth is identified, consisting of areas of dense cellularity interspersed with less dense myxoid regions. The cells show diffuse S-100 immunoreactivity. Which of the following is the most likely diagnosis?

A. Glioblastoma
B. Meningioma
C. Metastatic lung adenocarcinoma
D. Optic glioma
E. Schwannoma

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A. Glioblastoma (10%)
B. Meningioma (13%)
C. Metastatic lung adenocarcinoma (3%)
D. Optic glioma (1%)
✓ E. Schwannoma (70%)

Correct
70% Answered correctly
34 secs Time Spent
02/15/2021 Last Updated

Explanation



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**Schwannomas** are tumors of the peripheral nervous system that arise from Schwann cells. Microscopically, they appear biphasic with highly cellular areas (Antoni A pattern) intermixed with myxoid regions of low cellularity (Antoni B pattern). The Antoni A areas are composed of spindle cells with **elongated, wavy nuclei** that form palisading patterns with interspersing nuclear-free zones called Verocay bodies. Schwannomas are universally **S-100 positive** due to their neural crest cell origin. Another important S-100 positive tumor is melanoma (also derived from the neural crest).

Schwann cells are to the peripheral nervous system as oligodendrocytes are to the central nervous system: both protect and insulate axons. The transition from oligodendrocytes to Schwann cells occurs within a few millimeters from the surface of the brain and spinal cord. Therefore, schwannomas can occur within the cranial vault and spinal canal. Schwannomas may arise from any cranial nerve except the optic nerve (CN II) and olfactory nerve (CN I), which are not covered by Schwann cells.

The most common site of intracranial schwannomas is the **cerebellopontine angle** at CN VIII. Schwannomas in this particular location are also called acoustic neuromas, and can present with **tinnitus, vertigo**, and sensorineural **hearing loss**.

**(Choice A)** Glioblastoma is a highly aggressive primary brain tumor that consists of bizarre-looking glial cells with multiple mitotic figures, pseudopalisading necrosis, and abundant neovascularization and


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Exhibit Display

Schwannoma

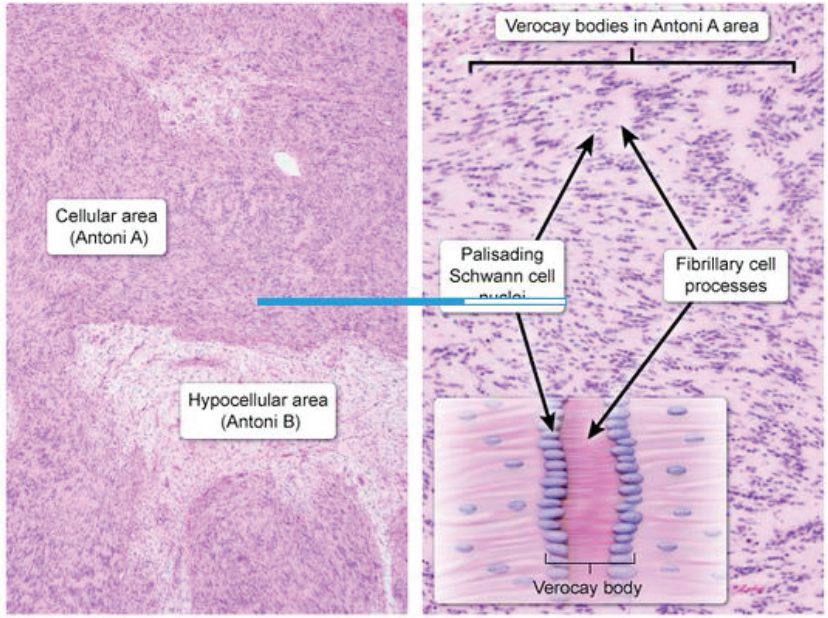


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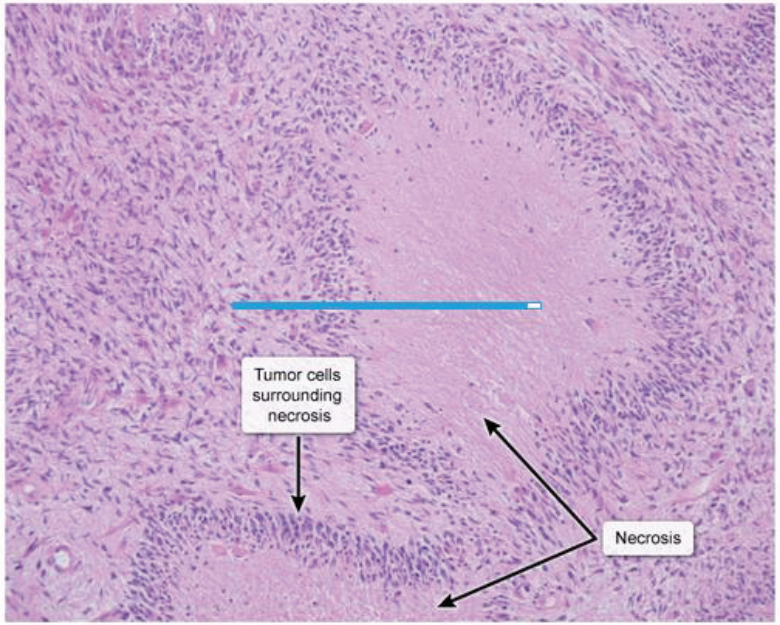
Exhibit Display

Glioblastoma

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cells with multiple mitotic figures, pseudopalisading necrosis, and abundant neovascularization and hemorrhage. It commonly occurs in the frontotemporoparietal white matter and grows along the white matter tracts across the corpus callosum to affect the opposite hemisphere.

**(Choice B)** Meningiomas are typically slow-growing extra-axial tumors that arise from the meningothelial cells of the arachnoid. Meningiomas most commonly appear as cells arranged in lobules or whorls with or without psammoma bodies (laminar calcifications).

**(Choice C)** Brain metastases are the most common cause of intracranial tumors in adults. Lung, breast, skin (melanoma), and renal cancer are particularly likely to metastasize to the brain. Metastatic brain lesions typically form well-circumscribed masses along the grey-white junction. Histologically, there is often necrosis with surrounding areas of reactive gliosis and edema.

**(Choice D)** Optic glioma is a form of glioma that affects the optic nerve. It is often found in association with neurofibromatosis type 1. Histologic findings are usually consistent with pilocytic astrocytoma and include tumor cells with hairlike processes, microcystic areas, and Rosenthal fibers (elongated or corkscrew intracytoplasmic eosinophilic bundles).

**Educational objective:**
Schwannomas present histologically with a biphasic pattern of cellularity (Antoni A and B areas) and S-100 positivity (indicating neural crest origin). Schwannomas can arise from the peripheral nerves, nerve roots


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cells with multiple mitotic figures, pseudopalisading necrosis, and abundant neovascularization and

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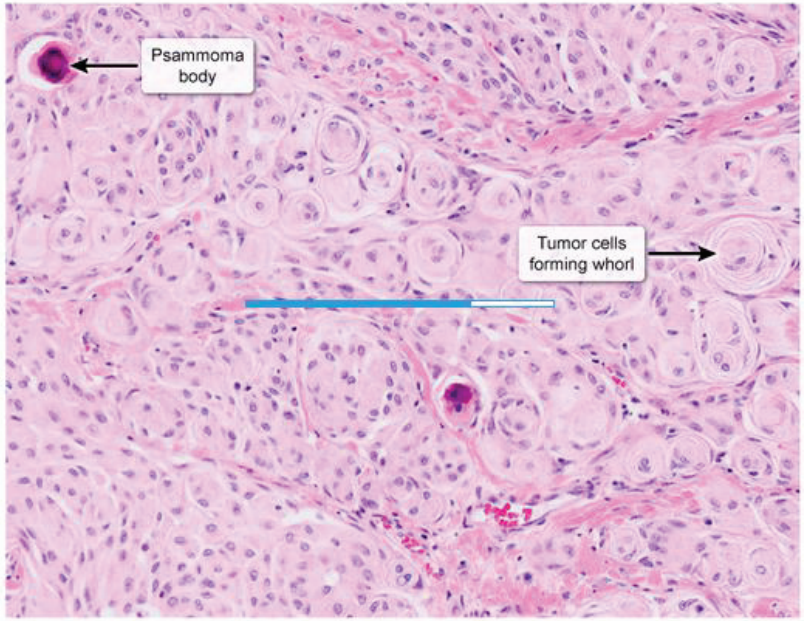
Meningioma

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positivity (indicating neural crest origin). Schwannomas can arise from the peripheral nerves, nerve roots



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**Educational objective:**

Schwannomas present histologically with a biphasic pattern of cellularity (Antoni A and B areas) and S-100 positivity (indicating neural crest origin). Schwannomas can arise from the peripheral nerves, nerve roots, and cranial nerves (except CN II and CN I). Acoustic neuromas are the most common type of intracranial schwannoma and are located at the cerebellopontine angle at CN VIII.

| Pathology | Nervous System | Vestibular schwannoma |
|---|---|---|
| Subject | System | Topic |

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A 57-year-old man is hospitalized for aspiration pneumonia. The patient was healthy and worked as an engineer without difficulty until about 4 months ago. Since that time, he has developed severe confusion, mood changes, and memory impairment and had to take medical leave from work. The patient is now completely dependent on his wife for toileting, feeding, and general self-care. Physical examination shows disorientation and sporadic, jerky extremity movements. During hospitalization, the patient lapses into a coma and dies. Postmortem examination of his brain shows widespread atrophy of the cerebral cortex and cerebellum. Histologic analysis of the patient's brain tissue would most likely show accumulation of which of the following?

A. Alpha-synuclein
B. Amyloid precursor protein
C. Phosphorylated tau
D. Protease-resistant protein
E. RNA virus



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A. Alpha-synuclein (12%)
B. Amyloid precursor protein (6%)
C. Phosphorylated tau (12%)
D. Protease-resistant protein (65%)
E. RNA virus (3%)

Incorrect
Correct answer

65%

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02/08/2021



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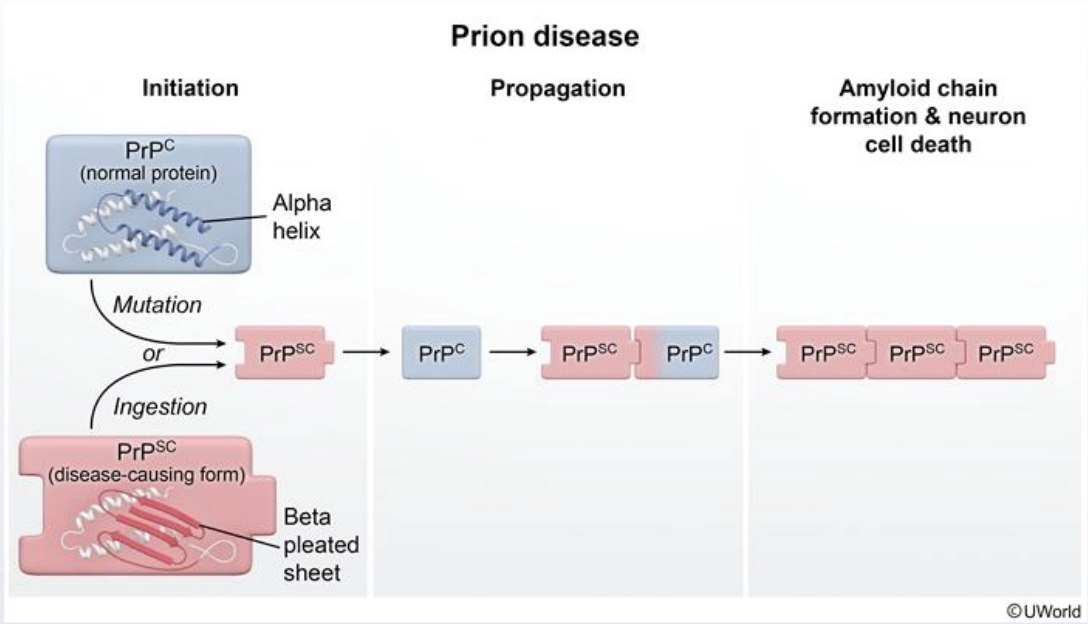


This previously healthy patient developed **rapidly progressive dementia** associated with **myoclonus** (eg, involuntary, jerky extremity movements) and brain atrophy (due to widespread neuronal loss). These findings are consistent with **Creutzfeldt-Jakob disease** (CJD), a rapidly fatal transmissible spongiform encephalopathy caused by prions.


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encephalopathy caused by prions.

Prion protein (PrP) is found in both neuronal and nonneuronal brain cells and normally exist in an **alpha-helical** structure ($PrP^{c}$). Prion disease occurs after a domain in this protein undergoes a conformational change from an alpha helix into a **beta pleated sheet** isoform ($PrP^{sc}$), which confers the ability to induce similar conformational changes in other proteins. This beta sheet conformation is **resistant to proteases** and forms long, highly **neurotoxic fibrils** that accumulate intracellularly in neurons and form extracellular deposits.

On microscopy, there is **spongiform degeneration** of the gray matter, which is characterized by formation of microscopic vacuoles within the neuronal processes. This leads to widespread **neuronal loss** and reactive gliosis without associated inflammation. This may be evident on imaging or gross pathology as widespread atrophy involving both the **cerebrum** and **cerebellum** (in contrast to many other neurodegenerative diseases that spare the cerebellum).

**(Choice A)** Cytoplasmic inclusions of alpha-synuclein are characteristic of dementia with Lewy bodies, which is characterized by visual hallucinations, parkinsonism, cognitive fluctuations, and REM sleep disorder.

**(Choice B)** Deposition of beta-amyloid occurs in Alzheimer dementia, which commonly presents with early


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**(Choice B)** Deposition of beta-amyloid occurs in Alzheimer dementia, which commonly presents with early and prominent memory impairment with language deficits and spatial disorientation. It is characterized by a slow (years to decades) decline in function until death.

**(Choice C)** Phosphorylated tau forms paired helical filaments that create intracellular neurofibrillary tangles. This is seen in both Alzheimer disease as well as frontotemporal dementia. Although memory impairment and behavioral changes can occur in these diseases, this patient's myoclonus and rapid progression leading to death are more consistent with CJD.

**(Choice E)** Prion diseases are the only known diseases that are transmissible by protein. Prion isoforms do not contain nucleic acids. Although HIV (an RNA virus) can cause dementia, it typically causes mild, subacute cognitive impairment without myoclonus.

**Educational objective:**

Creutzfeldt-Jakob disease is a prion disease characterized by rapidly progressive dementia, myoclonus, and death within a year of symptom onset. It is caused by the accumulation of an abnormally folded (ie, beta pleated sheet) protein that is resistant to proteases and can trigger similar conformational changes in other normally folded proteins.

**References**



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A 30-year-old man comes to the emergency department with sudden onset of severe headache and confusion. He has a history of autosomal dominant polycystic kidney disease. Neurological examination shows no meningeal signs or focal neurological deficits. CT scan of the head reveals blood in the subarachnoid space. The patient is admitted to the critical care unit for further management. On the fifth day after admission, he experiences new-onset weakness in the right arm and leg. Which of the following medications could have most likely prevented the neurological complications this patient developed in the hospital?

A. ACE inhibitor
B. Beta-adrenergic blocker
C. Calcium channel blocker
D. Central sympatholytic
E. Nitrate
F. Osmotic diuretic
G. Thiazide diuretic



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confusion. He has a history of autosomal dominant polycystic kidney disease. Neurological examination shows no meningeal signs or focal neurological deficits. CT scan of the head reveals blood in the subarachnoid space. The patient is admitted to the critical care unit for further management. On the fifth day after admission, he experiences new-onset weakness in the right arm and leg. Which of the following medications could have most likely prevented the neurological complications this patient developed in the hospital?

A. ACE inhibitor (8%)
B. Beta-adrenergic blocker (6%)
C. Calcium channel blocker (55%)
D. Central sympatholytic (4%)
E. Nitrate (4%)
F. Osmotic diuretic (18%)
G. Thiazide diuretic (2%)


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Explanation

This patient with **subarachnoid hemorrhage** (SAH) developed new-onset focal neurological deficits 5 days after his initial symptoms; a presentation characteristic of delayed cerebral ischemia due to cerebral vasospasm. SAH is most often caused by the rupture of a **saccular (berry) aneurysm**, which occurs frequently in patients with autosomal dominant polycystic disease.

**Cerebral vasospasm** with subsequent ischemia is the most common complication of SAH and typically manifests **3-12 days** after the initial incident with a change in mental status and/or new **focal neurological deficits**. Nimodipine, a selective **calcium channel blocker**, improves outcomes in patients with SAH by preventing or reducing the extent of ischemic neurological deficits caused by cerebral vasospasm. This **neuroprotective** effect is likely due to a combination of increased cerebral vasodilation and decreased calcium-dependent excitotoxicity.

**(Choices A and B)** Enalapril (an ACE inhibitor) and labetalol (a beta-adrenergic blocker with some alpha-antagonist activity) can be used to control hypertension (lowering the chance of rebleeding) in patients after SAH. However, rebleeding usually occurs in the first 24 hours after SAH, and acute onset of new neurological deficits 5 days after SAH is more indicative of delayed ischemia due to cerebral vasospasm.

**(Choice D)** Central sympatholytics (eg, methyldopa, clonidine) stimulate alpha-2A receptors centrally.



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**(Choice D)** Central sympatholytics (eg, methyldopa, clonidine) stimulate alpha-2A receptors centrally, resulting in a decrease in generalized sympathetic outflow and reduced blood pressure. They do not have a role in prevention of ischemic deficits due to cerebral vasospasm following SAH.

**(Choice E)** Nitrates (eg, nitroglycerin, isosorbide mononitrate) are used as vasodilators primarily for the treatment of angina pectoris. In patients with a recent SAH, nitrates should be avoided because they can increase cerebral blood flow and intracranial pressure, which can worsen bleeding.

**(Choice F)** Osmotic diuretics (eg, mannitol) are part of the treatment for increased intracranial pressure (ICP). Although hydrocephalus can be a complication of SAH and result in elevated ICP, it typically presents with a gradual change in level of consciousness accompanied by ocular changes (eg, downward eye deviation, miosis) rather than focal extremity deficits. Ventricular dilation on neuroimaging is diagnostic.

**(Choice G)** Thiazide diuretics are a first-line therapy for essential hypertension in the outpatient setting. They are not indicated for use in preventing complications due to cerebral vasospasm following SAH.

**Educational objective:**
Delayed cerebral ischemia due to cerebral vasospasm usually presents 3-12 days after the initial subarachnoid hemorrhage (SAH) with an acute change in mental status and/or new focal neurological


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treatment of angina pectoris. In patients with a recent SAH, nitrates should be avoided because they can increase cerebral blood flow and intracranial pressure, which can worsen bleeding.

**(Choice F)** Osmotic diuretics (eg, mannitol) are part of the treatment for increased intracranial pressure (ICP). Although hydrocephalus can be a complication of SAH and result in elevated ICP, it typically presents with a gradual change in level of consciousness accompanied by ocular changes (eg, downward eye deviation, miosis) rather than focal extremity deficits. Ventricular dilation on neuroimaging is diagnostic.

**(Choice G)** Thiazide diuretics are a first-line therapy for essential hypertension in the outpatient setting. They are not indicated for use in preventing complications due to cerebral vasospasm following SAH.

**Educational objective:**

Delayed cerebral ischemia due to cerebral vasospasm usually presents 3-12 days after the initial subarachnoid hemorrhage (SAH) with an acute change in mental status and/or new focal neurological deficits. Nimodipine, a selective calcium channel blocker, improves outcomes in patients with cerebral vasospasm by inducing cerebral vasodilation and decreasing calcium-dependent excitotoxicity.

**References**

- Nimodipine and its use in cerebrovascular disease: evidence from recent preclinical and controlled



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A 62-year-old woman comes to the office due to tingling and numbness in her feet over the last several months. The patient has also noticed a small ulcer on her right foot that "doesn't seem to be healing." Medical history is significant for long-term diabetes, hypertension, and gout. Physical examination shows decreased pain sensation over both feet and bilateral absence of ankle reflexes. This patient's neurological symptoms are most likely associated with which of the following features?

A. Endoneurial arteriole hyalinization
B. Endoneurial inflammatory infiltration
C. Mutation of a myelin protein gene
D. Nerve compression within an anatomic compartment
E. Poor signal transmission at the neuromuscular junction

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A 62-year-old woman comes to the office due to tingling and numbness in her feet over the last several months. The patient has also noticed a small ulcer on her right foot that "doesn't seem to be healing." Medical history is significant for long-term diabetes, hypertension, and gout. Physical examination shows decreased pain sensation over both feet and bilateral absence of ankle reflexes. This patient's neurological symptoms are most likely associated with which of the following features?

- A. Endoneurial arteriole hyalinization (74%)
- B. Endoneurial inflammatory infiltration (14%)
- C. ~~Mutation of a myelin protein gene~~ (0%)
- D. ~~Nerve compression within an anatomic compartment~~ (2%)
- E. ~~Poor signal transmission at the neuromuscular junction~~ (7%)

Correct

74%
Answered correctly

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01/03/2021
Last Updated



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| Diabetic neuropathy | |
|---|---|
| **Risk factors** | • Long duration of disease<br>• Chronic hyperglycemia/poor glycemic control |
| **Pathogenesis** | • Accumulation of glycosylation end products and sorbitol → altered metabolism and increased oxidative stress<br>• Occlusion of vasa nervorum with nerve ischemia<br>• Length-dependent axonopathy |
| **Clinical manifestations** | • **Peripheral polyneuropathy**: numbness, stocking-glove paresthesia, decreased proprioception<br>• **Autonomic neuropathy**: gastroparesis, orthostasis, neurogenic bladder, erectile dysfunction<br>• **Motor neuropathy**: distal limb weakness, hammer/claw toe deformities |

This patient with long-standing diabetes has numbness and tingling in her feet and reduced ankle reflexes bilaterally. This presentation suggests **diabetic neuropathy**, a common complication of diabetes mellitus


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This patient with long-standing diabetes has numbness and tingling in her feet and reduced ankle reflexes bilaterally. This presentation suggests **diabetic neuropathy**, a common complication of diabetes mellitus that is associated with poor glycemic control and/or long disease duration. It often manifests as a length-dependent **peripheral polyneuropathy** that primarily affects sensory axons; patients typically develop a **stocking-and-glove pattern** of pain or paresthesia. Diminished pain sensation coupled with poor wound healing predisposes diabetic patients to develop **nonhealing wounds**.

Neuronal injury in diabetes mellitus is multifactorial but largely occurs through the following mechanisms:

- Nonenzymatic glycosylation of tissue proteins (eg, nerve, vasa nervorum) results in **hyalinization of endoneurial arterioles**, leading to narrowing of the arteriole lumens and **ischemic nerve damage**. Additionally, glycosylation end-products are directly toxic to nerve tissue.
- Intracellular hyperglycemia occurs in peripheral nerves and results in increased metabolism of glucose into sorbitol by aldose reductase. Sorbitol accumulation increases cell osmolality, facilitates water influx into the cell, and **promotes oxidative stress** within the nerve.

**(Choice B)** Endoneurial inflammatory infiltration of the peripheral nerves is characteristic of Guillain-Barré syndrome, which typically causes a rapidly progressive ascending paralysis rather than a slowly progressive paresthesia. Segmental demyelination is another typical pathologic finding


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**(Choice B)** Endoneurial inflammatory infiltration of the peripheral nerves is characteristic of Guillain-Barré syndrome, which typically causes a rapidly progressive ascending paralysis rather than a slowly progressive paresthesia. Segmental demyelination is another typical pathologic finding.

**(Choice C)** Myelin protein gene mutations are involved in the pathogenesis of Charcot-Marie-Tooth disease, which presents with weakness of foot dorsiflexion due to involvement of the common peroneal nerve; sensory symptoms are typically less prominent.

**(Choice D)** Entrapment of a nerve within an anatomic compartment leads to compression neuropathy. The most common example is carpal tunnel syndrome, which occurs due to compression of the median nerve at the wrist.

**(Choice E)** Abnormal signal transmission at the neuromuscular junction is characteristic of myasthenia gravis (MG), which occurs due to antibodies against acetylcholine receptors, and Lambert-Eaton syndrome (LES), which occurs due to antibodies against presynaptic calcium channels. MG causes fatigable weakness that is most prominent in the proximal and facial muscles, while LES results in weakness that improves with repetition.

**Educational objective:**
Diabetic peripheral neuropathy is characterized by numbness and paresthesia in a stocking-and-glove


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disease, which presents with weakness of foot dorsiflexion due to involvement of the common peroneal nerve; sensory symptoms are typically less prominent.

**(Choice D)** Entrapment of a nerve within an anatomic compartment leads to compression neuropathy. The most common example is carpal tunnel syndrome, which occurs due to compression of the median nerve at the wrist.

**(Choice E)** Abnormal signal transmission at the neuromuscular junction is characteristic of myasthenia gravis (MG), which occurs due to antibodies against acetylcholine receptors, and Lambert-Eaton syndrome (LES), which occurs due to antibodies against presynaptic calcium channels. MG causes fatigable weakness that is most prominent in the proximal and facial muscles, while LES results in weakness that improves with repetition.

**Educational objective:**
Diabetic peripheral neuropathy is characterized by numbness and paresthesia in a stocking-and-glove distribution. It results from nonenzymatic glycosylation of proteins, leading to hyalinization of endoneurial arteries and ischemic nerve damage. In addition, accumulation toxic substances within neurons results in deranged metabolism and increased oxidative stress.


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An 8-year-old boy is being evaluated due to drug-resistant epilepsy. The patient has had recurrent seizures since age 2, which have remained uncontrolled despite multiple antiepileptic medications. He has no history of head trauma, meningitis, or encephalitis. There is no family history of seizure disorder. Electroencephalography reveals epileptic foci originating from the left temporal lobe, and neuroimaging reveals an abnormality of the left hippocampus. Surgical resection of the cortical region from which the seizure originates is performed. Histopathological examination of the removed brain tissue is most likely to reveal which of the following findings?

A. Astrocytic proliferation
B. Hemosiderin-laden macrophages
C. Microglial nodules
D. Neuronal inclusion bodies
E. Spongiform changes

Submit



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An 8-year-old boy is being evaluated due to drug-resistant epilepsy. The patient has had recurrent seizures since age 2, which have remained uncontrolled despite multiple antiepileptic medications. He has no history of head trauma, meningitis, or encephalitis. There is no family history of seizure disorder. Electroencephalography reveals epileptic foci originating from the left temporal lobe, and neuroimaging reveals an abnormality of the left hippocampus. Surgical resection of the cortical region from which the seizure originates is performed. Histopathological examination of the removed brain tissue is most likely to reveal which of the following findings?

- A. Astrocytic proliferation (51%)
- B. ~~Hemosiderin-laden macrophages~~ (2%)
- C. Microglial nodules (19%)
- D. Neuronal inclusion bodies (21%)
- E. Spongiform changes (5%)

Incorrect



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| Temporal lobe epilepsy | |
|---|---|
| **Etiology** | • Hippocampal sclerosis (most common)<br>• Other: infection, head trauma, tumors, congenital malformations |
| **Manifestations** | • Focal seizures with impaired awareness<br>• Secondary generalized seizures may occur<br>• Aura and automatisms are common |
| **Diagnostic studies** | • EEG: epileptiform waves in the temporal region<br>• MRI: Hippocampal atrophy |
| **Histopathology** | • Atrophy of the hippocampal neurons with reactive gliosis |

**EEG** = electroencephalography.

This patient with recurrent seizures has an epileptogenic focus in the temporal lobe, **suggesting temporal lobe epilepsy** (TLE), the most common type of localization-related (ie, focal) epilepsy. Localization epilepsies occur when partial seizures originate from one area of the brain and are usually due to an underlying structural disorder which serves as an epileptogenic focus. In the case of TLE, this is most


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**EEG** = electroencephalography.

This patient with recurrent seizures has an epileptogenic focus in the temporal lobe, **suggesting temporal lobe epilepsy** (TLE), the most common type of localization-related (ie, focal) epilepsy. Localization epilepsies occur when partial seizures originate from one area of the brain and are usually due to an underlying structural disorder which serves as an epileptogenic focus. In the case of TLE, this is most commonly due to **hippocampal sclerosis**, which is usually visible as hippocampal atrophy on MRI.

The pathogenesis of hippocampal sclerosis is incompletely understood but may in some cases be related to prior prolonged febrile seizures, particularly in patients with an underlying genetic predisposition. This results in the characteristic histopathologic findings of **atrophy of the hippocampal neurons** with marked reactive gliosis (**astrocyte proliferation** in response to injury). Surgical resection may reduce or cure seizures associated with TLE.

**(Choice B)** Hemosiderin-laden macrophages are associated with prior intracerebral hemorrhage, which may cause seizures but typically presents acutely with altered mental status and focal neurologic deficits. Neuroimaging would demonstrate expanding blood, not a focal abnormality in the hippocampus.

**(Choice C)** Microglial nodules form when cells of microglia surround a neuron and phagocytize it. The nodules are most commonly seen in viral CNS infection (particularly HIV) and are not typically associated


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EEG = electroencephalography

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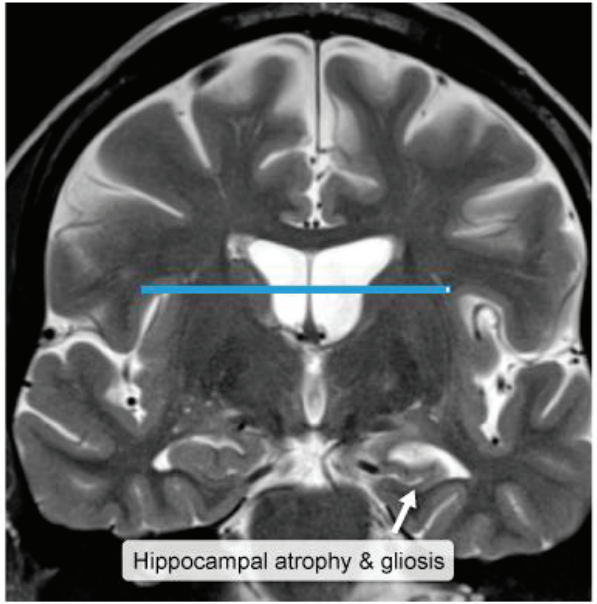
## Mesial temporal sclerosis

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Neuroimaging would demonstrate expanding blood, not a focal abnormality in the hippocampus.

**(Choice C)** Microglial nodules form when cells of microglia surround a neuron and phagocytize it. The nodules are most commonly seen in viral CNS infection (particularly HIV) and are not typically associated with TLE.

**(Choice D)** Neuronal inclusion bodies are often seen in frontotemporal dementia (characterized by prominent personality/behavioral changes and atrophy of the frontal and temporal lobes on neuroimaging) and Parkinson disease (characterized by bradykinesia, rigidity, pill-rolling tremor, and dementia). These disorders occur in elderly patients and are not associated with seizures.

**(Choice E)** Spongiform changes occur in prion diseases (eg, Creutzfeldt-Jacob, kuru). Patients have progressive tremors, ataxia, and dementia. Electroencephalography reveals periodic sharp-wave complexes, not focal epileptiform discharges, and hippocampal abnormalities are unexpected.

**Educational objective:**
Temporal lobe epilepsy is most commonly due to hippocampal sclerosis. Histopathology of hippocampal sclerosis demonstrates atrophy of the hippocampal neurons with marked reactive gliosis (astrocyte proliferation in response to injury).

Pathology Nervous System Seizures



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A 70-year-old woman with a history of unilateral extremity weakness and seizures is found unresponsive at home by her home health care nurse. On arrival of emergency medical services, she is found to have no pulse or spontaneous respirations and is declared dead. Autopsy shows a large thrombus occluding the left anterior descending coronary artery. Additional cerebral findings are shown in the exhibit. Which of the following most accurately describes the pathogenesis of this patient's brain lesion?

A. Fibroblast proliferation in the affected area

B. Granulomatous reaction against parasites

C. Immune-mediated focal demyelination

D. Necrosis of rapidly dividing, anaplastic astrocytes

E. Tissue destruction by lysosomal enzymes

Submit



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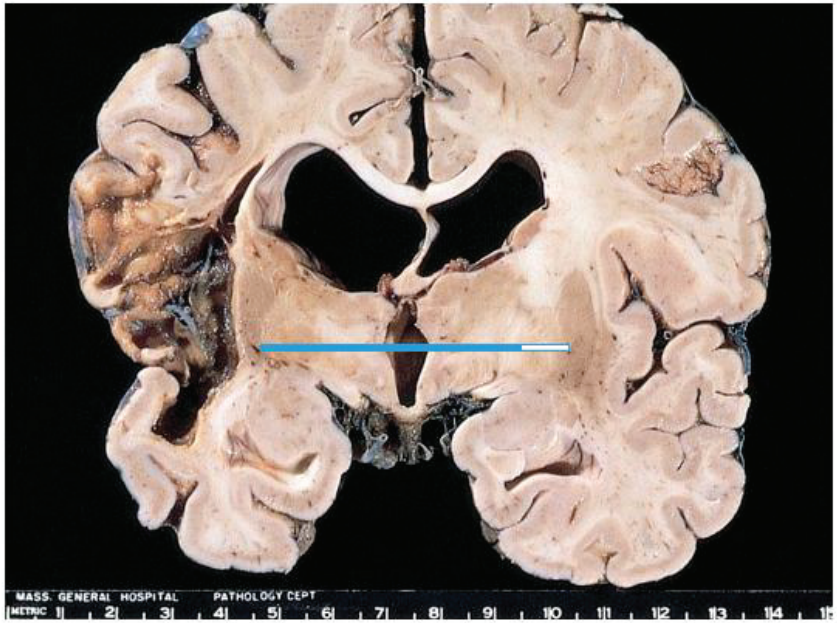


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A 70-year-old woman with a history of unilateral extremity weakness and seizures is found unresponsive at home by her home health care nurse. On arrival of emergency medical services, she is found to have no pulse or spontaneous respirations and is declared dead. Autopsy shows a large thrombus occluding the left anterior descending coronary artery. Additional cerebral findings are shown in the exhibit. Which of the following most accurately describes the pathogenesis of this patient's brain lesion?

A. Fibroblast proliferation in the affected area (7%)
B. ~~Granulomatous reaction against parasites~~ (0%)
C. ~~Immune-mediated focal demyelination~~ (1%)
D. ~~Necrosis of rapidly dividing, anaplastic astrocytes~~ (16%)
✓ E. Tissue destruction by lysosomal enzymes (73%)

Correct

73%
Answered correctly

01 min, 04 secs
Time Spent

01/21/2021
Last Updated



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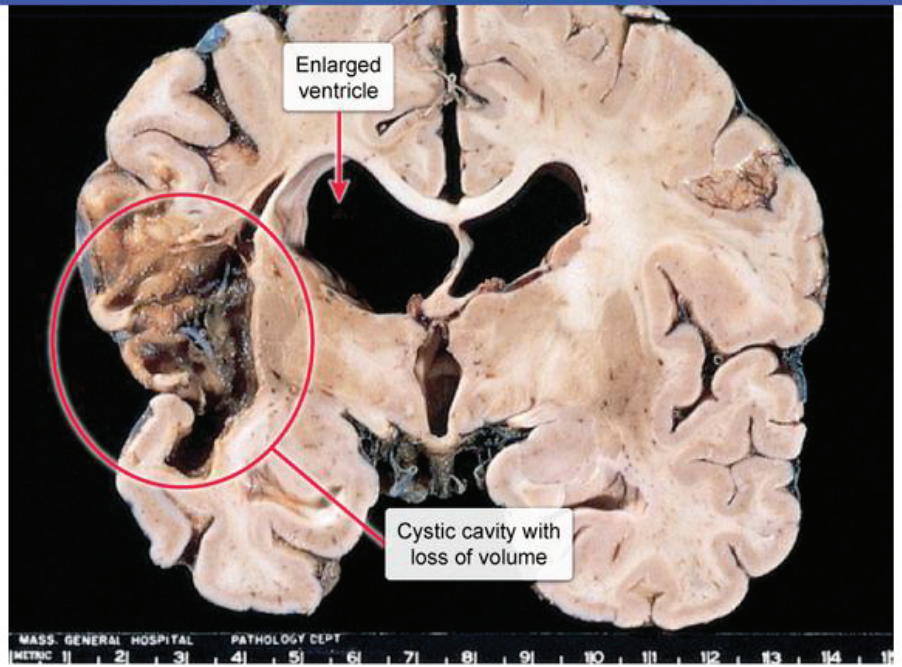


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The autopsy image shows a coronal section of the brain with evidence of past necrosis (eg, cystic cavity, volume loss, and enlarged ventricle). These findings are consistent with an **old cerebral infarct**, which was likely responsible for this patient's chronic neurologic symptoms (eg, extremity weakness and seizures).

Interruption in blood supply to an area of the brain, such as by thrombosis or embolism, induces irreversible ischemic changes in neurons. Release of **lysosomal enzymes** from ischemic neurons and responding inflammatory cells (eg, neutrophils, macrophages) results in tissue degradation in the affected region **(liquefactive necrosis)**. Over time, phagocytic cells remove the necrotic tissue, leaving a cavity, while astrocytes proliferate around the periphery to form a scar (gliosis).

Liquefactive necrosis is characteristic of irreversible CNS injury because of the brain's high cholesterol content and lack of supporting architecture. It also occurs in other body tissues in the setting of severe infection/inflammation (eg, bacterial abscess, fungal infection) because of the release of hydrolytic enzymes from reacting inflammatory cells.

**(Choice A)** Early fibroblast migration to an area of injury occurs outside of the CNS and results in the formation of granulation tissue and fibrous scarring. In the CNS, tissue repair and scar formation are performed by astrocytes.



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performed by astrocytes.

**(Choice B)** A granulomatous reaction against parasites within the CNS occurs in neurocysticercosis. However, multiple cystic lesions or residual calcified granulomas would be expected.

**(Choice C)** Multiple sclerosis is a chronic inflammatory demyelinating disease characterized grossly by multiple periventricular lesions (ie, demyelinating plaques). Cystic cavity formation does not occur.

**(Choice D)** Although glioblastoma multiforme can present with areas of cystic necrosis on gross examination, these areas classically are part of a diffuse, poorly delineated, heterogenous mass with midline shift away from the affected tissue.

**Educational objective:**
Liquefactive necrosis is characterized by complete digestion and removal of necrotic tissue with formation of a cystic cavity. Irreversible ischemic CNS injury is typically followed by liquefactive necrosis due to the release of lysosomal enzymes from inflammatory cells and damaged neurons.

| Pathology | Nervous System | Necrosis |
|---|---|---|
| Subject | System | Topic |

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performed by astrocytes.

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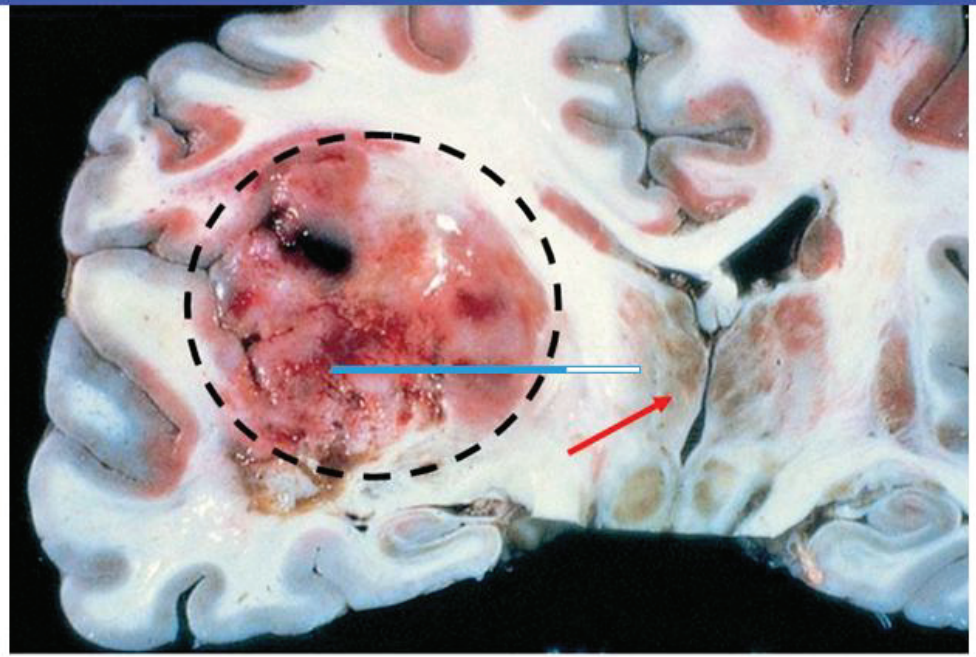

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A 38-year-old woman comes to the emergency department due to severe headache. An hour ago, she experienced a sudden, explosive headache followed by a brief loss of consciousness. Since regaining consciousness spontaneously, she has had persistent global headache and nausea. Head movement or bright light worsens the pain. Temperature is 37.2 C (99 F), blood pressure is 142/90 mm Hg, and pulse is 98/min. The patient is somnolent but easily rouses to voice. She is well oriented to time, place, and person. There is increased resistance to neck flexion, which elicits pain. The pupils are equal and reactive to light. Deep tendon reflexes and sensory examination are normal. Brain imaging would most likely reveal which of the following?

A. Blood layering the cerebral sulci
B. Diffuse cerebral edema
C. Intracerebral hemorrhage
D. Large vessel thrombosis
E. Scattered cerebral emboli



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experienced a sudden, explosive headache followed by a brief loss of consciousness. Since regaining consciousness spontaneously, she has had persistent global headache and nausea. Head movement or bright light worsens the pain. Temperature is 37.2 C (99 F), blood pressure is 142/90 mm Hg, and pulse is 98/min. The patient is somnolent but easily rouses to voice. She is well oriented to time, place, and person. There is increased resistance to neck flexion, which elicits pain. The pupils are equal and reactive to light. Deep tendon reflexes and sensory examination are normal. Brain imaging would most likely reveal which of the following?

- A. Blood layering the cerebral sulci (58%)
- B. ~~Diffuse cerebral edema~~ (9%)
- C. Intracerebral hemorrhage (29%)
- D. ~~Large vessel thrombosis~~ (2%)
- E. ~~Scattered cerebral emboli~~ (0%)

Correct

58%

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02/15/2021



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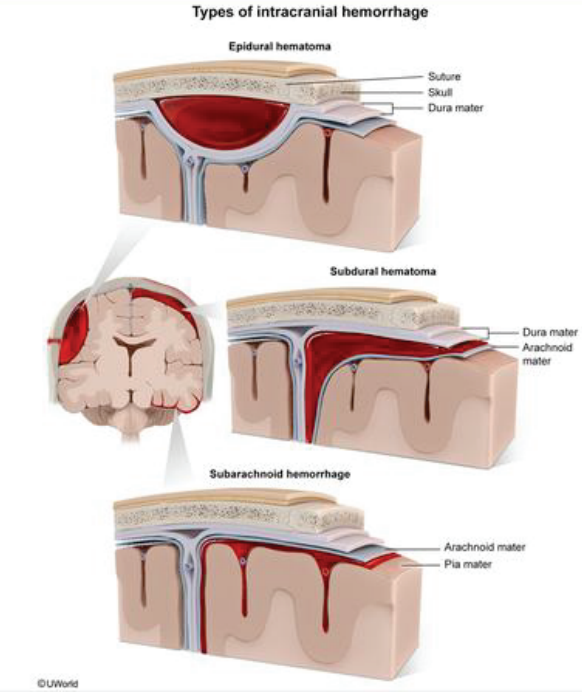


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This patient with a sudden-onset, explosive headache (ie, **thunderclap headache**), brief loss of consciousness, and signs of **meningeal irritation** (eg, neck stiffness, pain) likely has a **subarachnoid hemorrhage** (SAH). SAH usually results from the spontaneous rupture of a **saccular (berry) aneurysm**. These aneurysms most commonly develop at branch points of the anterior, middle, or posterior cerebral arteries in patients with a genetic predisposition (eg, family history, autosomal dominant polycystic kidney disease, Ehlers-Danlos syndrome). Blood empties into the subarachnoid space and **pools in the cerebral sulci and basal cisterns**, which is the diagnostic finding of SAH on CT scan.

Blood in direct contact with the pia mater triggers severe headache and meningeal irritation. Nausea, photophobia, and transient loss of consciousness are also common. Many patients appear neurologically intact at presentation; however, progressively **deteriorating mental status** (eg, somnolence) is typical. In addition, SAH commonly triggers delayed cerebral vasospasm (eg, 4 days after initial bleeding) resulting in stroke with focal neurologic deficits.

**(Choice B)** Diffuse cerebral edema can result from too-rapid correction of hypernatremia. The drop in serum osmolarity stimulates water flow into brain cells, which can increase intracranial pressure to cause impaired cerebral perfusion and eventual brain herniation.

**(Choice C)** Intracerebral hemorrhage usually results from the rupture of small arteries in the pons, thalamus, or basal ganglia, commonly in the setting of underlying hypertensive vasculopathy. The


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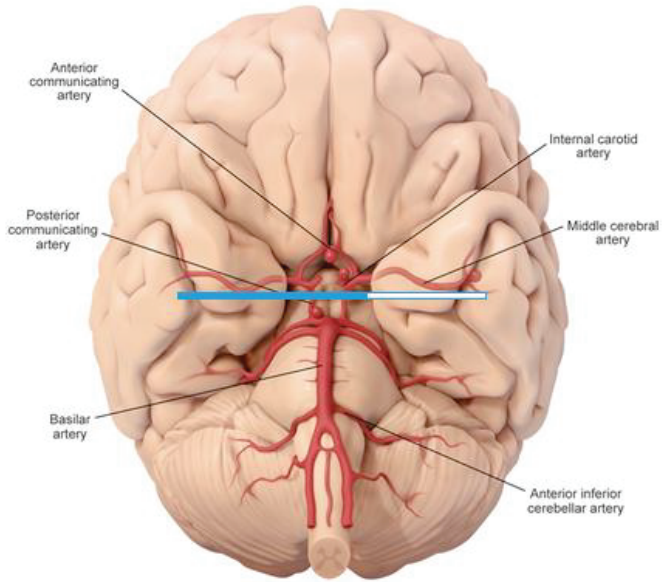
This patient with a sudden-onset, explosive headache (ie, **thunderclap headache**), brief loss of

Exhibit Display

Common locations of berry (saccular) aneurysms

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thalamus, or basal ganglia, commonly in the setting of underlying hypertensive vasculopathy. The



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This patient with a sudden-onset, explosive headache (ie, **thunderclap headache**), brief loss of

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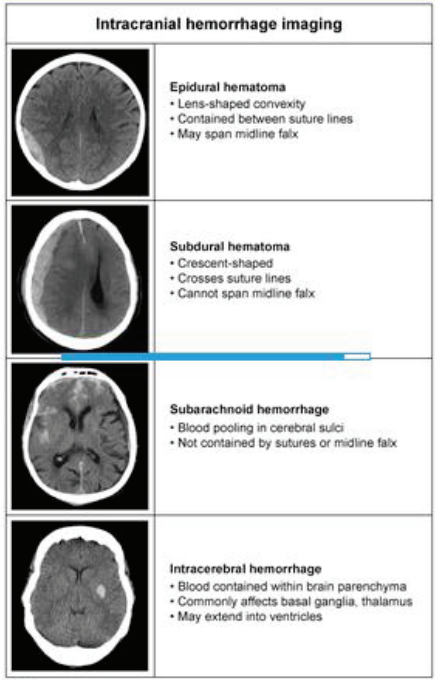


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thalamus, or basal ganglia, commonly in the setting of underlying hypertensive vasculopathy. The


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impaired cerebral perfusion and eventual brain herniation.

**(Choice C)** Intracerebral hemorrhage usually results from the rupture of small arteries in the pons, thalamus, or basal ganglia, commonly in the setting of underlying hypertensive vasculopathy. The hemorrhage occurs within the brain parenchyma, with patients usually experiencing focal neurologic deficits. Severe headache is sometimes present, but meningeal signs are not expected.

**(Choices D and E)** Plaque rupture and thrombosis of a large cerebral artery (eg, anterior cerebral artery) and embolization of thrombus (eg, cardioembolic thrombus due to atrial fibrillation) are common mechanisms of ischemic stroke. Patients usually have focal neurologic deficits without headache or meningeal signs.

**Educational objective:**
Sudden-onset, severe headache with signs of meningeal irritation (eg, neck pain, stiffness) should raise suspicion for subarachnoid hemorrhage (SAH). SAH usually results from rupture of a saccular (berry) aneurysm, and it is recognized on CT scan by blood pooling in the cerebral sulci and basal cisterns.

| Pathology | Nervous System | Subarachnoid hemorrhage |
|---|---|---|
| Subject | System | Topic |



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A 54-year-old man is brought to the office by his friend because of worsening memory impairment over the past several months. The patient is also withdrawn and not focused during conversations. He is slow to answer questions or carry out instructions. The patient has a prolonged history of HIV infection and has had several opportunistic infections due to inconsistent antiretroviral medication use. On physical examination, he is alert and oriented. Muscle strength, deep tendon reflexes, and sensation are normal. MRI of the head shows diffuse cerebral atrophy with no focal mass lesions or areas of demyelination. Viral proliferation in which of the following central nervous system cells is most likely involved in this patient's disease process?

A. $CD4^+$ helper T cells
B. Cortical neurons
C. Endothelial cells
D. Macrophages
E. Oligodendrocytes



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past several months. The patient is also withdrawn and not focused during conversations. He is slow to answer questions or carry out instructions. The patient has a prolonged history of HIV infection and has had several opportunistic infections due to inconsistent antiretroviral medication use. On physical examination, he is alert and oriented. Muscle strength, deep tendon reflexes, and sensation are normal. MRI of the head shows diffuse cerebral atrophy with no focal mass lesions or areas of demyelination. Viral proliferation in which of the following central nervous system cells is most likely involved in this patient's disease process?

A. $CD4^+$ helper T cells (16%)
B. Cortical neurons (22%)
C. Endothelial cells (2%)
D. Macrophages (38%)
E. Oligodendrocytes (20%)

Correct
38%
01 min, 03 secs
03/14/2021


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In the context of a long history of HIV infection, this patient's memory impairment, subcortical dysfunction (ie, inattention, impaired psychomotor speed), and cerebral atrophy on MRI of the head are consistent with **HIV-associated dementia (HAD)**. HAD is characteristically a subcortical dementia with prominent mood, attention, memory, and psychomotor dysfunction. It is uncommon in patients receiving antiretroviral treatment but can occur in those with inconsistently treated, advanced HIV infection.

Although HIV-1 preferentially infects and replicates in $CD4^+$ helper T cells in peripheral blood **(Choice A)**, CNS infection is associated with a change in viral tropism (ie, ability to infect different cell types) to microglia and **macrophages**, which allows the virus to penetrate deeper into the brain parenchyma. This macrophage tropic **(M-tropic)** version of the virus becomes "**compartmentalized**" in the CNS and evolves independently from the strain found in the blood.

**(Choices B and E)** HIV is not neuron or oligodendrocyte tropic. Viruses that are neuron tropic include the lyssaviruses that cause rabies.

**(Choice C)** HIV does not preferentially infect and replicate in endothelial cells in the CNS. Cytomegalovirus is an example of an endothelial cell–tropic virus.

**Educational objective:**

HIV-associated dementia has become rare since the advent of antiretroviral treatment but may still develop


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Although HIV-1 preferentially infects and replicates in CD4+ helper T cells in peripheral blood **(Choice A)**, CNS infection is associated with a change in viral tropism (ie, ability to infect different cell types) to microglia and **macrophages**, which allows the virus to penetrate deeper into the brain parenchyma. This macrophage tropic **(M-tropic)** version of the virus becomes "**compartmentalized**" in the CNS and evolves independently from the strain found in the blood.

**(Choices B and E)** HIV is not neuron or oligodendrocyte tropic. Viruses that are neuron tropic include the lyssaviruses that cause rabies.

**(Choice C)** HIV does not preferentially infect and replicate in endothelial cells in the CNS. Cytomegalovirus is an example of an endothelial cell–tropic virus.

**Educational objective:**
HIV-associated dementia has become rare since the advent of antiretroviral treatment but may still develop in patients with inadequately treated, late-stage HIV infection. In the CNS, HIV preferentially infects and replicates in macrophages.

**References**

- Macrophage cell-cell interactions promoting HIV-1 infection.



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www.ncbi.nlm.nih.gov/pubmed/32354203

A 56-year-old woman is brought to the emergency department due to several days of progressive dyspnea, productive cough, and fever. Today, her son found her very short of breath and obtunded. The patient has a history of hypertension, type 2 diabetes mellitus, and long-standing rheumatoid arthritis. Examination reveals bilateral pneumonia and severe respiratory distress. The patient is lethargic without focal neurologic deficits. Urgent endotracheal intubation is performed for mechanical ventilation, and the patient is started on broad-spectrum antibiotics. Repeat examination 2 hours later shows that she has developed areflexic, flaccid paralysis of all extremities. Which of the following is the most likely cause of the neurologic deficits in this patient?

A. Cerebral septic emboli
B. Diabetic neuropathy
C. Guillain-Barré syndrome
D. Malignant hyperthermia
E. Vertebral subluxation


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productive cough, and fever. Today, her son found her very short of breath and obtunded. The patient has a history of hypertension, type 2 diabetes mellitus, and long-standing rheumatoid arthritis. Examination reveals bilateral pneumonia and severe respiratory distress. The patient is lethargic without focal neurologic deficits. Urgent endotracheal intubation is performed for mechanical ventilation, and the patient is started on broad-spectrum antibiotics. Repeat examination 2 hours later shows that she has developed areflexic, flaccid paralysis of all extremities. Which of the following is the most likely cause of the neurologic deficits in this patient?

A. Cerebral septic emboli (24%)
B. Diabetic neuropathy (1%)
C. Guillain-Barré syndrome (30%)
D. Malignant hyperthermia (9%)
✓ E. Vertebral subluxation (33%)

Correct

33%
47 secs
01/11/2021



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This patient with **rheumatoid arthritis** underwent urgent endotracheal intubation due to severe pneumonia and subsequently developed sudden-onset quadriparesis. Long-standing rheumatoid arthritis frequently involves the **cervical spine** and causes joint destruction with vertebral malalignment (**subluxation**). The atlantoaxial joint is most often involved as the atlas (C1) has a high degree of mobility relative to the axis (C2 odontoid and body).

Chronic symptoms of cervical subluxation include neck pain, stiffness, and neurologic findings (eg, sensory loss, muscle weakness). **Endotracheal intubation** can **acutely worsen** the subluxation and cause **compression of the spinal cord** and/or vertebral arteries. Acute spinal cord injury results in flaccid paralysis with decreased or absent reflexes below the level of the compression due to spinal shock; the paralysis eventually becomes spastic as spinal shock resolves over the ensuing days to weeks.

**(Choice A)** Cerebral septic emboli are usually due to infective endocarditis of the left-sided heart valves. Patients can develop acute neurologic findings including unilateral paralysis; quadriparesis would be less likely. This patient also has no cardiac murmur or other stigmata (eg, petechiae, splinter hemorrhages) to suggest endocarditis.

**(Choice B)** Diabetic neuropathy presents with a slowly progressive decrease in vibratory sensation, proprioception, and temperature sensation. Early neuropathy can cause decreased ankle reflexes,


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suggest endocarditis.

**(Choice B)** Diabetic neuropathy presents with a slowly progressive decrease in vibratory sensation, proprioception, and temperature sensation. Early neuropathy can cause decreased ankle reflexes, whereas later disease can cause widespread loss of reflexes with motor weakness.

**(Choice C)** Guillain-Barré syndrome presents with progressively worsening, symmetrical, flaccid muscle weakness with absent or decreased reflexes. The abnormalities typically start in the lower extremities and ascend upward over the course of days to weeks.

**(Choice D)** Malignant hyperthermia is usually due to anesthesia exposure (eg, halothane, succinylcholine), causing increased and sustained muscle contraction with myocyte breakdown. Patients typically develop diffuse muscle rigidity followed by hyperthermia and possible myoglobinuria.

**Educational objective:**
Long-standing rheumatoid arthritis can affect the cervical spine, causing vertebral malalignment (subluxation) that can affect the atlantoaxial joint. Extension of the neck during endotracheal intubation can worsen the subluxation, leading to acute compression of the spinal cord and/or vertebral arteries.

| Pathophysiology | Nervous System | Rheumatoid arthritis |
|---|---|---|
| Subject | System | Topic |

In an experiment, laboratory animals are subjected to a toxic insult that specifically targets the protein kinesin. Which of the following is most likely to be absent from tissues on histological examination as a result?

A. Nissl substance in pyramidal neurons
B. Secretory vesicles in nerve terminals
C. T-tubules in skeletal muscle cells
D. Desmosomes in epithelial lining cells
E. Microvilli in intestinal epithelial cells

Submit



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In an experiment, laboratory animals are subjected to a toxic insult that specifically targets the protein kinesin. Which of the following is most likely to be absent from tissues on histological examination as a result?

A. ~~Nissl substance in pyramidal neurons~~ (7%)

✓ B. Secretory vesicles in nerve terminals (58%)

C. ~~T-tubules in skeletal muscle cells~~ (14%)

D. ~~Desmosomes in epithelial lining cells~~ (6%)

E. Microvilli in intestinal epithelial cells (12%)

Correct

58% Answered correctly

55 secs Time Spent

01/30/2021 Last Updated

Explanation



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Explanation

Kinesin is a microtubule associated motor protein whose function is anterograde transport of intracellular vesicles and organelles toward the plus (rapidly growing) ends of microtubules. Kinesin uses energy derived from ATP hydrolysis to move along the microtubule. The plus ends of microtubules typically lie at sites distant from the nucleus; thus, in neurons, kinesin carries vesicles and organelles away from the cell body and toward the nerve terminal. A targeted toxic insult to this protein would be expected to impair anterograde transport resulting in a deficiency of synaptic vesicles at the nerve terminal.

**(Choice A)** The Nissl substance in neurons corresponds to the rough endoplasmic reticulum.

**(Choice C)** The transverse tubule (T-tubule) system is a tubular network located at the junction of the A and I bands of striated myocytes. T-tubules are open to the extracellular space and facilitate the spread of depolarization to the inside of the cell.

**(Choice D)** Desmosomes are protein aggregates that mediate cell-cell adhesion between epithelial cells.

**(Choice E)** Microvilli are small cylindrical extensions of the apical plasma membrane that contain actin thin filaments. Microvilli cover the apical surfaces of intestinal epithelial cells. They do not contain microtubules or microtubule associated proteins.


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**(Choice A)** The Nissl substance in neurons corresponds to the rough endoplasmic reticulum.

**(Choice C)** The transverse tubule (T-tubule) system is a tubular network located at the junction of the A and I bands of striated myocytes. T-tubules are open to the extracellular space and facilitate the spread of depolarization to the inside of the cell.

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**(Choice E)** Microvilli are small cylindrical extensions of the apical plasma membrane that contain actin thin filaments. Microvilli cover the apical surfaces of intestinal epithelial cells. They do not contain microtubules or microtubule associated proteins.

**Educational Objective:**
Kinesin is a microtubule-associated, ATP-powered motor protein that facilitates the anterograde transport of neurotransmitter-containing secretory vesicles down axons to synaptic terminals.

| Histology | Nervous System | Neuronal physiology |
|---|---|---|
| Subject | System | Topic |

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A 3-year-old girl is brought to the office due to leg stiffness. Her mother reports that the patient is a clumsy walker and requires assistance to ambulate. The patient was born preterm and has delayed developmental skills. Physical examination shows increased knee and ankle reflexes and clonus at the ankles bilaterally. Muscle tone of the upper extremities and neck is also mildly increased. MRI of the brain reveals periventricular leukomalacia suggestive of cerebral palsy. An oral medication is prescribed that reduces the extremity stiffness. Which of the following CNS drug effects most likely resulted in this patient's improvement?

A. Activation of NMDA glutamate receptors
B. Agonistic activity at GABA receptors
C. Blockade of acetylcholine muscarinic receptors
D. Blockade of receptors for glycine
E. Increased dopaminergic activity

Submit



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A 3-year-old girl is brought to the office due to leg stiffness. Her mother reports that the patient is a clumsy walker and requires assistance to ambulate. The patient was born preterm and has delayed developmental skills. Physical examination shows increased knee and ankle reflexes and clonus at the ankles bilaterally. Muscle tone of the upper extremities and neck is also mildly increased. MRI of the brain reveals periventricular leukomalacia suggestive of cerebral palsy. An oral medication is prescribed that reduces the extremity stiffness. Which of the following CNS drug effects most likely resulted in this patient's improvement?

A. Activation of NMDA glutamate receptors (6%)
B. Agonistic activity at GABA receptors (62%)
C. Blockade of acetylcholine muscarinic receptors (13%)
D. Blockade of receptors for glycine (6%)
E. Increased dopaminergic activity (11%)

62%  01 min, 36 secs  11/23/2020


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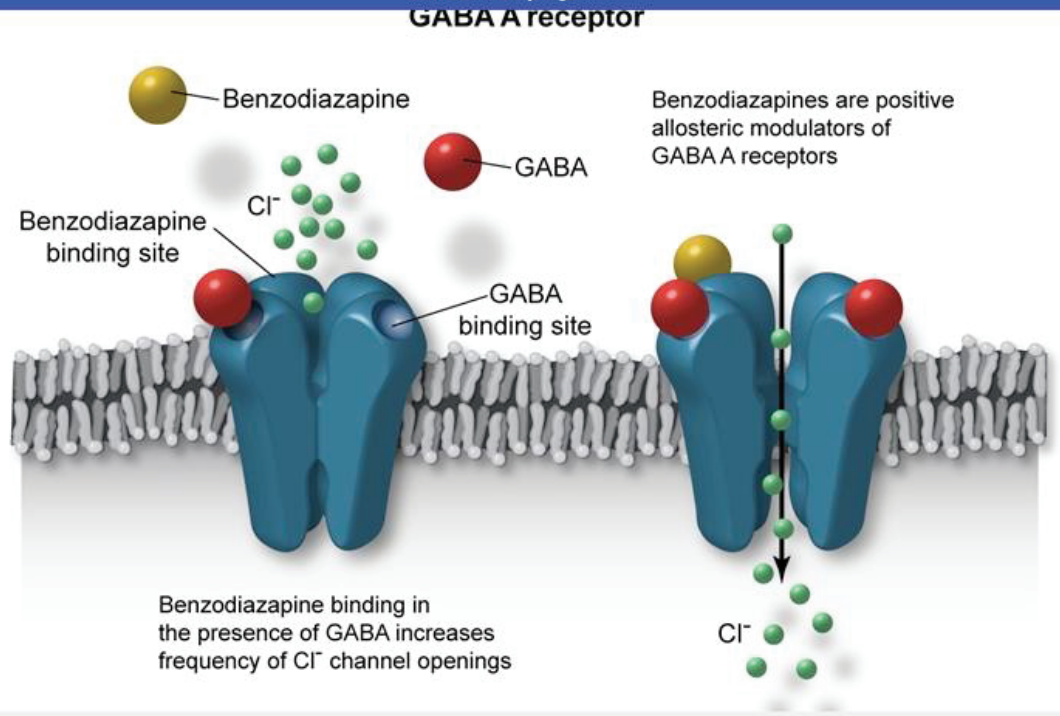


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This patient has cerebral palsy, a heterogeneous condition characterized by permanent, nonprogressive motor dysfunction caused by damage to the developing brain. Certain subtypes (eg, spastic cerebral palsy) often manifest as delayed gross motor milestones and **spasticity** (eg, hypertonia, hyperreflexia). Spastic cerebral palsy may be caused by white matter necrosis (seen in this patient as periventricular leukomalacia), which leads to a **loss of descending inhibitory control** from the upper motor neurons. This results in muscle overactivity, leading to increased tone and hyperreflexia.

Enhancement of CNS inhibitory neurotransmitter activity can improve spasticity. **GABA** is the primary **inhibitory neurotransmitter** in the CNS and acts on two different receptors:

- **GABA A** receptor mediates a fast response to GABA because it is an ion-gated chloride channel. Activation of this receptor leads to rapid muscle relaxation and sedation. Its activity is enhanced by **benzodiazepines**, which can be used to treat spasticity.
- **GABA B** receptor mediates a slower response to GABA because it is mediated by a G protein–coupled receptor that opens potassium channels. It is agonized by **baclofen**, which can also be used to treat spasticity.

**(Choice A)** Glutamate is the primary excitatory CNS neurotransmitter; therefore, activation of NMDA glutamate receptors would result in increased excitation and lead to further increases in muscle tone.


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to treat spasticity.

**(Choice A)** Glutamate is the primary excitatory CNS neurotransmitter; therefore, activation of NMDA glutamate receptors would result in increased excitation and lead to further increases in muscle tone.

**(Choices C and E)** Dopamine is a modulatory (rather than primarily excitatory or inhibitory) neurotransmitter that affects motor control. In patients with Parkinson disease who have a relative deficiency of dopamine in the substantia nigra, medications that increase dopaminergic activity (eg, levodopa) can improve muscle rigidity. In some patients, a relative excess of acetylcholine compared to dopamine has been implicated in the tremor or rigidity associated with Parkinson disease or drug-induced parkinsonism. In these patients, anticholinergic medications (eg, trihexyphenidyl) are sometimes used.

**(Choice D)** Glycine is an inhibitory neurotransmitter found primarily in the spinal cord rather than in the brain. Blockade of glycine receptors (eg, strychnine poisoning) leads to increased muscle contraction.

**Educational objective:**
Cerebral palsy results in spasticity (eg, hypertonia, hyperreflexia) due to a loss of descending inhibitory control. Medications used to enhance the activity of GABA, the primary inhibitory neurotransmitter of the CNS, can improve spasticity.


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A 22-year-old man comes to the office due to occasional dull headaches that awaken him from sleep. The patient has no associated neurologic deficits. There is no history of migraines in the family. His temperature is 37.2 C (99 F), blood pressure is 140/80 mm Hg, pulse is 60/min, and respirations are 12/min. On physical examination, there are several 3- to 5-cm flat, pigmented spots on his trunk. There are also multiple, subcentimeter, soft, fleshy, cutaneous tumors located on his trunk and neck. The predominant cells forming these skin tumors most likely originated from which of the following structures?

- A. Endoderm
- B. Mesoderm
- C. Neural crest
- D. Neural tube
- E. Notochord
- F. Surface ectoderm

Submit



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A 22-year-old man comes to the office due to occasional dull headaches that awaken him from sleep. The patient has no associated neurologic deficits. There is no history of migraines in the family. His temperature is 37.2 C (99 F), blood pressure is 140/80 mm Hg, pulse is 60/min, and respirations are 12/min. On physical examination, there are several 3- to 5-cm flat, pigmented spots on his trunk. There are also multiple, subcentimeter, soft, fleshy, cutaneous tumors located on his trunk and neck. The predominant cells forming these skin tumors most likely originated from which of the following structures?

- A. ~~Endoderm~~ (1%)
- ✗ B. Mesoderm (3%)
- ✓ C. Neural crest (73%)
- D. Neural tube (3%)
- E. Notochord (0%)
- F. Surface ectoderm (17%)

Incorrect



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| Embryological derivatives | | |
|---|---|---|
| Ectoderm | Surface ectoderm | • Anterior pituitary (Rathke pouch)<br>• Lens & cornea<br>• Inner ear sensory organs, olfactory epithelium<br>• Nasal & oral epithelial linings, salivary glands<br>• Epidermis, sweat & mammary glands |
| | Neural tube | • Brain & spinal cord<br>• Posterior pituitary, pineal gland<br>• Retina |
| | Neural crest | • Neural ganglia, adrenal medulla<br>• Schwann cells; pia & arachnoid mater<br>• Aorticopulmonary septum & endocardial cushions<br>• Branchial arches (bones & cartilage)<br>• Skull bones<br>• Melanocytes |


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| | |
|---|---|
| Mesoderm | • Muscles (skeletal, cardiac & smooth)<br>• Connective tissue, bone & cartilage<br>• Serosal linings (eg, peritoneum)<br>• Cardiovascular & lymphatic system<br>• Spleen & hemopoietic cells<br>• Kidney & ureters, internal genitalia<br>• Adrenal cortex |
| Endoderm | • Gastrointestinal tract, liver, pancreas<br>• Lungs<br>• Thymus, parathyroids, thyroid follicular cells<br>• Middle ear epithelium<br>• Bladder & urethra<br>• Parafollicular (C) cells* |

*Formerly thought to be of neural crest origin.

This patient has clinical features of **neurofibromatosis type I** (von Recklinghausen disease), an autosomal dominant neurocutaneous disorder caused by mutations in the *NF1* tumor suppressor gene


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*Formerly thought to be of neural crest origin.

This patient has clinical features of **neurofibromatosis type I** (von Recklinghausen disease), an autosomal dominant neurocutaneous disorder caused by mutations in the *NF1* tumor suppressor gene. Patients typically develop hyperpigmented macules (café-au-lait spots) over the trunk soon after birth and are at increased risk of developing central nervous system neoplasms (eg, optic gliomas, pilocytic astrocytomas), which can cause elevated intracranial pressure and headache.

**Cutaneous neurofibromas** usually manifest during early adolescence as multiple, raised, fleshy tumors (<2 cm) that often increase in size and number with age. These are benign nerve sheath neoplasms predominantly comprised of **Schwann cells**, which are embryologically derived from the **neural crest**.

**(Choice A)** The endoderm gives rise to thyroid follicular cells (derived from the primitive tongue) and the epithelial linings of the gastrointestinal tract, middle ear, lung, bladder, and most of the urethra. It also gives rise to the bulk of the liver, pancreas, and lungs, as these structures form from outpouchings of the primitive gut tube.

**(Choice B)** The mesoderm is divided into paraxial, intermediate, and lateral sections and gives rise to muscles, bones, blood, connective tissue, dermis, and the kidneys/ureters.

**(Choice D)** The neural tube gives rise to neurons of the central nervous system and the neurohypophysis


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*Formerly thought to be of neural crest origin

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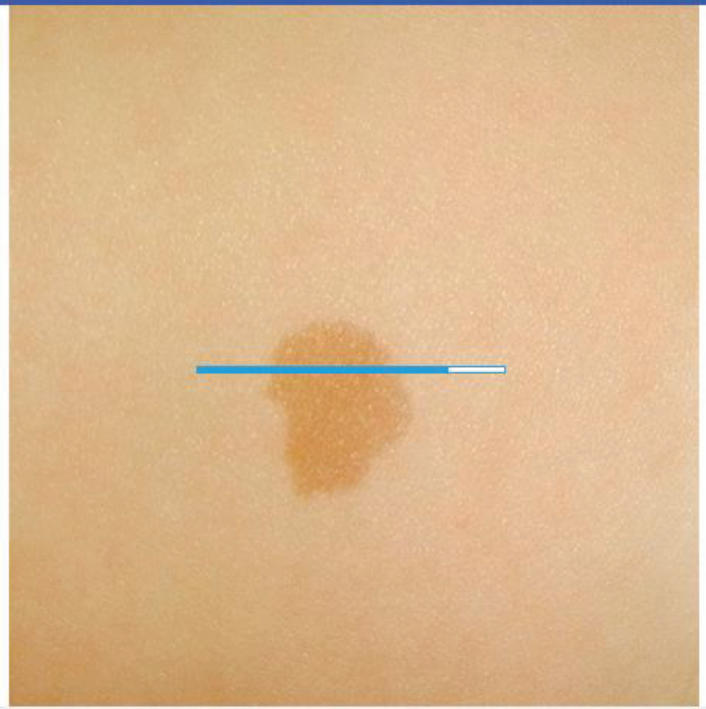

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[Choice D] The neural tube gives rise to neurons of the central nervous system and the neurohypophysis



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gives rise to the bulk of the liver, pancreas, and lungs, as these structures form from outpouchings of the primitive gut tube.

**(Choice B)** The mesoderm is divided into paraxial, intermediate, and lateral sections and gives rise to muscles, bones, blood, connective tissue, dermis, and the kidneys/ureters.

**(Choice D)** The neural tube gives rise to neurons of the central nervous system and the neurohypophysis, retina, pineal gland, preganglionic autonomic fibers, astrocytes, and ependymal cells.

**(Choice E)** The notochord almost completely regresses in humans, and its only major derivative is the nucleus pulposus of the intervertebral disc. Vertebrae are derived from the paraxial mesoderm.

**(Choice F)** The surface ectoderm gives rise to the epidermis, lens of the eye, outer layer of the cornea, nasal and oral epithelium, and anal epithelium below the dentate line.

**Educational objective:**

Neurofibromatosis type I (von Recklinghausen disease) is an autosomal dominant disorder caused by mutations in the *NF1* tumor suppressor gene. Patients characteristically develop numerous cutaneous neurofibromas comprised mostly of Schwann cells, which are embryologically derived from the neural crest.

**References**



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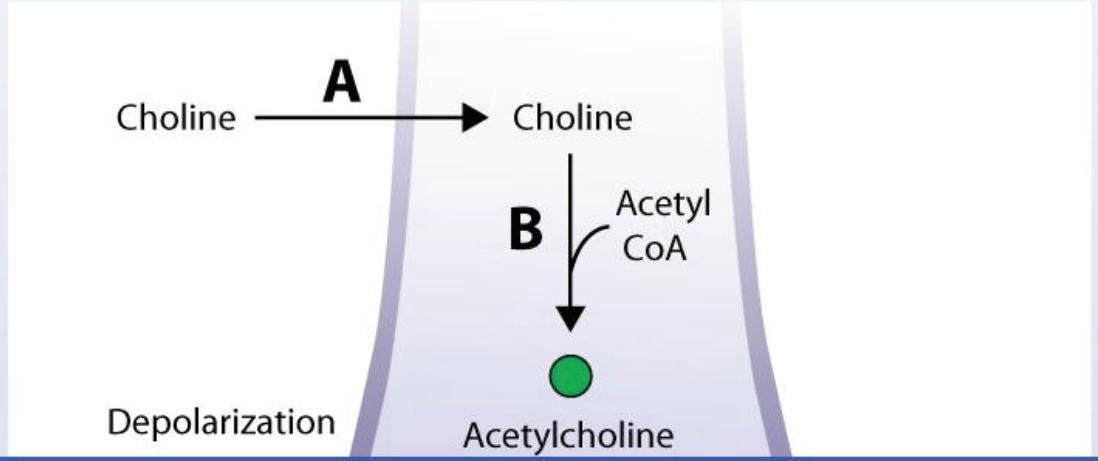
A 46-year-old man comes to the emergency department due to worsening blurry vision, difficulty swallowing, and dry mouth for the past hour. He has also been having nausea and abdominal discomfort but has no headache or fever. The patient has no prior medical conditions and takes no medications. He smokes a pack of cigarettes daily but does not use alcohol or illicit drugs. The patient has not traveled recently but attended a community potluck event yesterday where he sampled home-canned foods. Physical examination shows bilateral ptosis and sluggish pupillary response. Which of the following steps in neuromuscular transmission is most likely affected in this patient?





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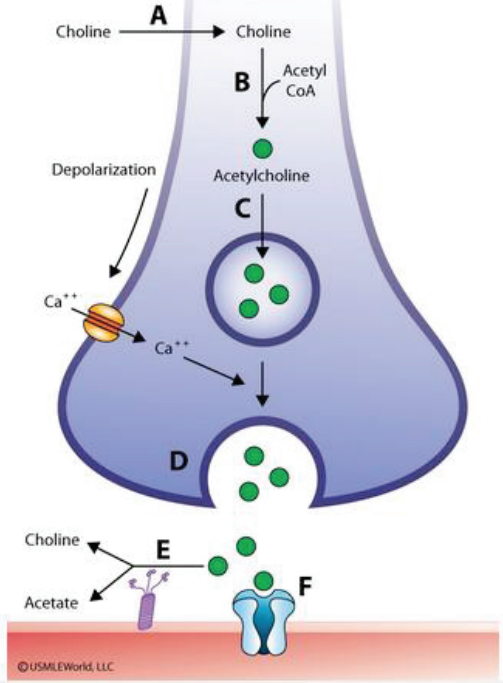


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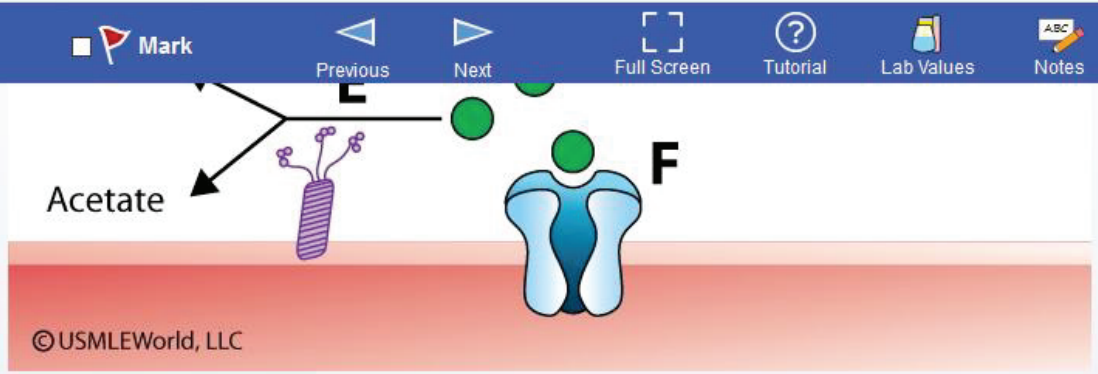


- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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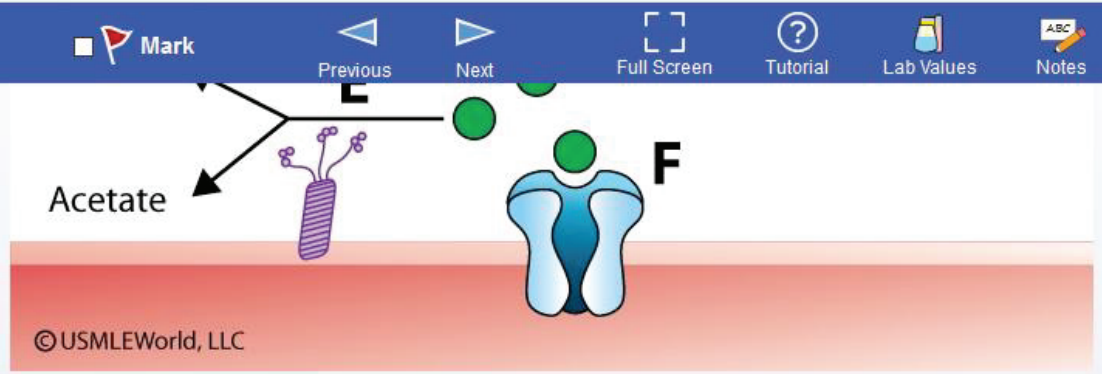


- A.A (0%)
- B.B (0%)
- C.C (4%)
- ✓ D.D (75%)
- E.E (7%)
- F. F (11%)

Correct

75%

01 min, 03 secs

02/20/2021



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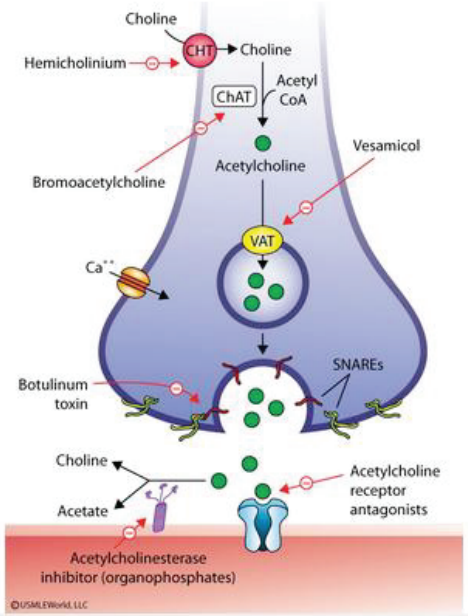
Inhibitors of acetylcholine neurotransmission

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This patient with gastrointestinal discomfort has manifestations of both **nicotinic** blockade (eg, dysphagia, ptosis) and **muscarinic blockade** (eg, dry mouth) that developed after eating home-canned food. This is strongly suggestive of food poisoning with ***Clostridium botulinum* toxin**, a preformed neurotoxin. Botulism characteristically presents as a symmetric, descending paralysis that first manifests with cranial nerve abnormalities (**diplopia, dysphagia, dysphonia ["3Ds"]**). Nausea, vomiting, and abdominal pain may also occur in foodborne botulism, which classically occurs 12-36 hours after consumption of contaminated, **home-canned foods**.

Botulinum toxin causes disease by inhibiting cholinergic nerves, including nicotinic and muscarinic motor neurons. It enters the nerve terminals through endocytosis, where it prevents binding and fusion of acetylcholine (ACh)-containing synaptic vesicles with the plasma membrane through the destruction of SNARE proteins. This effectively blocks ACh release into the neuromuscular synapse. Botulinum toxin is highly potent; a very small quantity can be lethal without ventilatory support. The toxin is **heat-labile**, so disease can be prevented by thoroughly heating food prior to consumption.

**(Choice A)** Hemicholinium blocks choline uptake by the presynaptic neuron, preventing ACh synthesis through depletion of intracellular choline.



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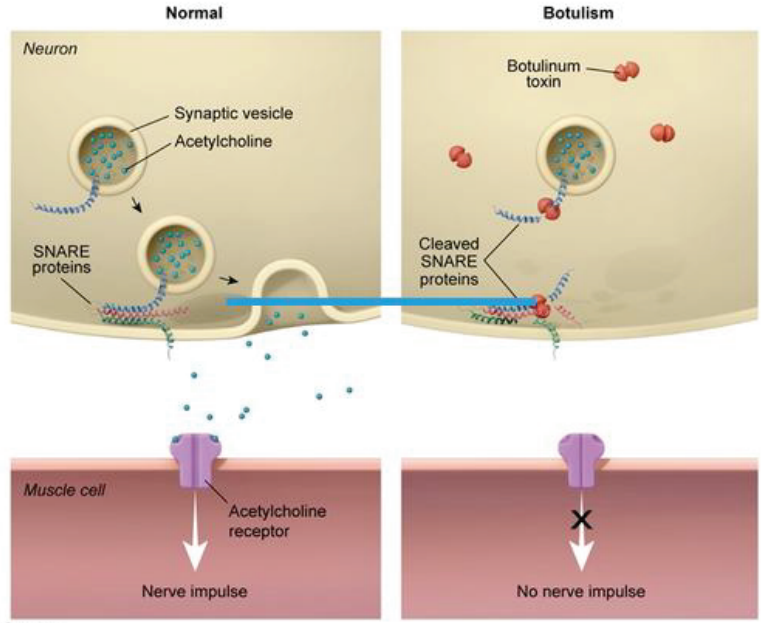
Botulism

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through depletion of intracellular choline.

**(Choice B)** Bromoacetylcholine inhibits choline acetyltransferase, blocking the synthesis of ACh from acetate and choline.

**(Choice C)** Vesamicol noncompetitively blocks the vesicular ACh transporter, preventing ACh from entering secretory vesicles in the presynaptic nerve terminal.

**(Choice E)** Acetylcholinesterase inhibitors such as organophosphates (commonly used as insecticides) prevent ACh breakdown. Manifestations of organophosphate poisoning reflect depolarizing blockade (eg, muscle weakness, fasciculations, paralysis), central nervous system effects (eg, lethargy, seizures), and muscarinic overstimulation (eg, miosis, bradycardia, increased lacrimation and salivation).

**(Choice F)** Anticholinergic poisoning due to competitive antagonists of muscarinic ACh receptors (eg, atropine, scopolamine) is relatively common and can manifest as cutaneous vasodilation, anhidrosis, hyperthermia, mydriasis, and delirium. However, these agents have no effect on the nicotinic ACh receptors controlling voluntary muscles. Poisoning due to **nicotinic** receptor antagonists (eg, pancuronium, tubocurarine) is uncommon as these agents have poor oral absorption.

**Educational objective:**
Botulinum toxin blocks the presynaptic exocytosis of ACh vesicles, causing impaired muscarinic and


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**(Choice B)** Bromo
acetate and choline

**(Choice C)** Vesam
entering secretory

**(Choice E)** Acetyl
prevent ACh breakd
muscle weakness,
muscarinic overstim

**(Choice F)** Antich
atropine, scopolam
hyperthermia, mydr
receptors controllin
pancuronium, tubo

**Educational objec**
Botulinum toxin blo

Exhibit Display

| Cholinergic toxicity | |
|---|---|
| Muscarinic effects **(DUMBELS)** | • **D**iarrhea/diaphoresis<br>• **U**rination<br>• **M**iosis<br>• **B**ronchospasm, bronchorrhea & bradycardia<br>• **E**mesis<br>• **L**acrimation<br>• **S**alivation |
| Nicotinic effects | • Muscle weakness, paralysis & fasciculations |

New | Existing



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**(Choice B)** Bromo
acetate and choline

**(Choice C)** Vesam
entering secretory

**(Choice E)** Acetyl
prevent ACh breakd
muscle weakness,
muscarinic overstim

**(Choice F)** Antich
atropine, scopolam
hyperthermia, mydr
receptors controllin
pancuronium, tubo

**Educational objec**
Botulinum toxin blo

Exhibit Display

| Anticholinergic toxicity | |
|---|---|
| **Symptom** | **Mechanism** |
| **"Hot as a hare"**<br>↑ Body temperature | • ↓ Sweating leads to ↓ heat dissipation |
| **"Dry as a bone"**<br>↓ Secretions (eg, mucous membranes, sweat glands) | • ↓ Glandular secretion & smooth muscle contraction |
| **"Red as a beet"**<br>Flushed skin | • Superficial vasodilation from ↑ body heat |
| **"Blind as a bat"**<br>Cycloplegia, mydriasis | • Paralysis of ciliary muscle & iris sphincter |
| **"Mad as a hatter"**<br>Altered mental status | • Permeates blood-brain barrier & affects CNS pathways |
| **"Full as a flask"**<br>Constipation, urinary retention | • ↓ Intestinal smooth muscle contraction<br>• ↓ Detrusor contraction & ↓ internal urethral sphincter relaxation |
| **"Fast as a fiddle"** | |

New | Existing



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**(Choice B)** Bromo
acetate and choline

**(Choice C)** Vesam
entering secretory

**(Choice E)** Acetyl
prevent ACh break
muscle weakness,
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**(Choice F)** Antich
atropine, scopolam
hyperthermia, mydr
receptors controllin
pancuronium, tubo

**Educational objec**
Botulinum toxin blo

Exhibit Display

| Symptom | Mechanism |
|---|---|
| **"Hot as a hare"**<br>↑ Body temperature | • ↓ Sweating leads to ↓ heat dissipation |
| **"Dry as a bone"**<br>↓ Secretions (eg, mucous membranes, sweat glands) | • ↓ Glandular secretion & smooth muscle contraction |
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| **"Blind as a bat"**<br>Cycloplegia, mydriasis | • Paralysis of ciliary muscle & iris sphincter |
| **"Mad as a hatter"**<br>Altered mental status | • Permeates blood-brain barrier & affects CNS pathways |
| **"Full as a flask"**<br>Constipation, urinary retention | • ↓ Intestinal smooth muscle contraction<br>• ↓ Detrusor contraction & ↓ internal urethral sphincter relaxation |
| **"Fast as a fiddle"**<br>Tachycardia | • ↓ Vagal tone at the sinoatrial node |

New | Existing



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prevent ACh breakdown. Manifestations of organophosphate poisoning reflect depolarizing blockade (eg, muscle weakness, fasciculations, paralysis), central nervous system effects (eg, lethargy, seizures), and muscarinic overstimulation (eg, miosis, bradycardia, increased lacrimation and salivation).

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**Educational objective:**

Botulinum toxin blocks the presynaptic exocytosis of ACh vesicles, causing impaired muscarinic and nicotinic neurotransmission; it characteristically presents as a symmetric, descending paralysis that first manifests with cranial nerve abnormalities, often following consumption of home-canned foods.

**References**

- Large outbreak of botulism associated with a church potluck meal—Ohio, 2015.

Microbiology Nervous System Botulism



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A 31-year-old female with new-onset generalized tonic-clonic seizures has an intracranial mass detected on head CT scan. Biopsy of the mass reveals neoplastic cells that stain positive for synaptophysin and negative for glial fibrillary acidic protein. These neoplastic cells most likely originate from the same precursor tissue as which of the following?

A. Astrocytes
B. Oligodendroglia
C. Ependymal cells
D. Meningothelial cells
E. Neurons

Submit



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A 31-year-old female with new-onset generalized tonic-clonic seizures has an intracranial mass detected on head CT scan. Biopsy of the mass reveals neoplastic cells that stain positive for synaptophysin and negative for glial fibrillary acidic protein. These neoplastic cells most likely originate from the same precursor tissue as which of the following?

- A. Astrocytes (12%)
- B. Oligodendroglia (17%)
- C. Ependymal cells (11%)
- D. Meningothelial cells (16%)
- ✓ E. Neurons (42%)

Correct

42% Answered correctly

59 secs Time Spent

01/30/2021 Last Updated

Explanation



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Synaptophysin is a transmembrane glycoprotein found in the presynaptic vesicles of neurons, neuroectodermal and neuroendocrine cells. Immunoreactivity of a CNS tumor for synaptophysin indicates a neuronal origin (Choice E). Such neoplasms are rare and compose less than 1% of CNS tumors. The majority of primary CNS tumors in adults are of glial origin, meningiomas and pituitary adenomas are the next most common. Primary tumors in adults tend to be supratentorial while those in children tend to lie below the tentorium. Metastatic disease to the CNS occurs more commonly than primary CNS tumors.

Unlike tumors of neuronal origin, gliomas stain positively for glial fibrillary acidic protein (GFAP). Immunoreactivity for GFAP is characteristic for astrocytomas including glioblastoma multiforme, oligodendrogliomas, ependymomas and peripheral neural sheath tumors.

**(Choices A, B and C)** Astrocytes, oligodendrocytes, and ependymal cells give rise to tumors collectively referred to as gliomas (astrocytomas, oligodendrogliomas and ependymomas, respectively). Cells from tumors of glial origin stain positively for glial fibrillary acidic protein (GFAP).

**(Choice D)** Cells of the arachnoid villi give rise to meningiomas, most of which are benign. These tumors are diagnosed by imaging; they do not stain for GFAP or synaptophysin.

**Educational Objective:**

Synaptophysin is a protein found in the presynaptic vesicles of neurons, neuroendocrine and


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Unlike tumors of neuronal origin, gliomas stain positively for glial fibrillary acidic protein (GFAP). Immunoreactivity for GFAP is characteristic for astrocytomas including glioblastoma multiforme, oligodendrogliomas, ependymomas and peripheral neural sheath tumors.

**(Choices A, B and C)** Astrocytes, oligodendrocytes, and ependymal cells give rise to tumors collectively referred to as gliomas (astrocytomas, oligodendrogliomas and ependymomas, respectively). Cells from tumors of glial origin stain positively for glial fibrillary acidic protein (GFAP).

**(Choice D)** Cells of the arachnoid villi give rise to meningiomas, most of which are benign. These tumors are diagnosed by imaging; they do not stain for GFAP or synaptophysin.

**Educational Objective:**
Synaptophysin is a protein found in the presynaptic vesicles of neurons, neuroendocrine and neuroectodermal cells. CNS tumors of neuronal origin frequently stain positively for synaptophysin on immunohistology. Neoplasms of glial origin (astrocytomas, ependymomas, and oligodendrogliomas) stain for GFAP.

| Pathology | Nervous System | Brain tumors |
|---|---|---|
| Subject | System | Topic |


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A 23-year-old woman is brought to the emergency department unconscious after a motor vehicle accident. The patient was texting on her cell phone and was not wearing a seatbelt during the incident. She has no known medical problems and takes no medications. Her temperature is 36.7 C (98 F), blood pressure is 155/90 mm Hg, pulse is 62/min, and respirations are 10/min. A linear skull fracture at the junction of the frontal, parietal, temporal, and sphenoid bones is seen on head CT scan. A branch of which of the following arteries is most likely severed in this patient?

A. Facial
B. Maxillary
C. Middle cerebral
D. Occipital
E. Ophthalmic
F. Sphenopalatine

Submit



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A 23-year-old woman is brought to the emergency department unconscious after a motor vehicle accident. The patient was texting on her cell phone and was not wearing a seatbelt during the incident. She has no known medical problems and takes no medications. Her temperature is 36.7 C (98 F), blood pressure is 155/90 mm Hg, pulse is 62/min, and respirations are 10/min. A linear skull fracture at the junction of the frontal, parietal, temporal, and sphenoid bones is seen on head CT scan. A branch of which of the following arteries is most likely severed in this patient?

- A. Facial (10%)
- ✓ B. Maxillary (47%)
- C. Middle cerebral (28%)
- D. Occipital (1%)
- E. Ophthalmic (4%)
- F. Sphenopalatine (6%)


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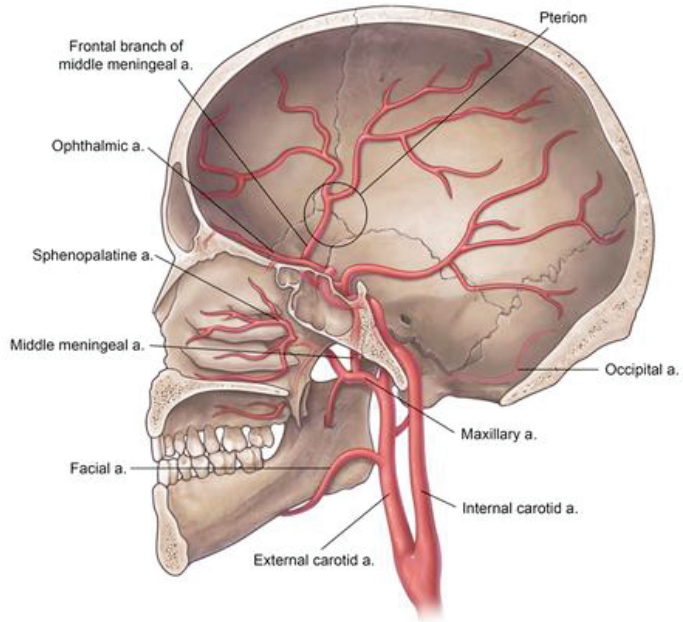
Arteries of the Head

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This patient has suffered a **fracture** at the **pterion**, a region where the frontal, parietal, temporal, and sphenoid bones meet in the skull. The bone is thin in this region, and fractures there risk lacerating the **middle meningeal artery** and causing an epidural hematoma. Epidural hematomas require prompt treatment as they are under systemic arterial pressure and can expand rapidly, leading to elevated intracranial pressure (can cause Cushing reflex), brain herniation (eg, uncal herniation with oculomotor nerve palsy), and death.

The middle meningeal artery is a branch of the **maxillary artery** (one of the terminal branches of the external carotid artery), which enters the skull at the foramen spinosum and supplies the dura mater and periosteum.

**(Choice A)** The facial artery is a branch of the external carotid artery, which courses over the mandible anterior to the insertion of the masseter muscle to supply the oral, nasal, and buccal regions.

**(Choice C)** The middle cerebral artery is a branch of the internal carotid artery and supplies much of the parietal and temporal regions of the brain. Injury to this artery or its branches can cause subarachnoid or intracerebral hemorrhage.

**(Choice D)** The occipital artery arises opposite the facial artery from the external carotid, coursing



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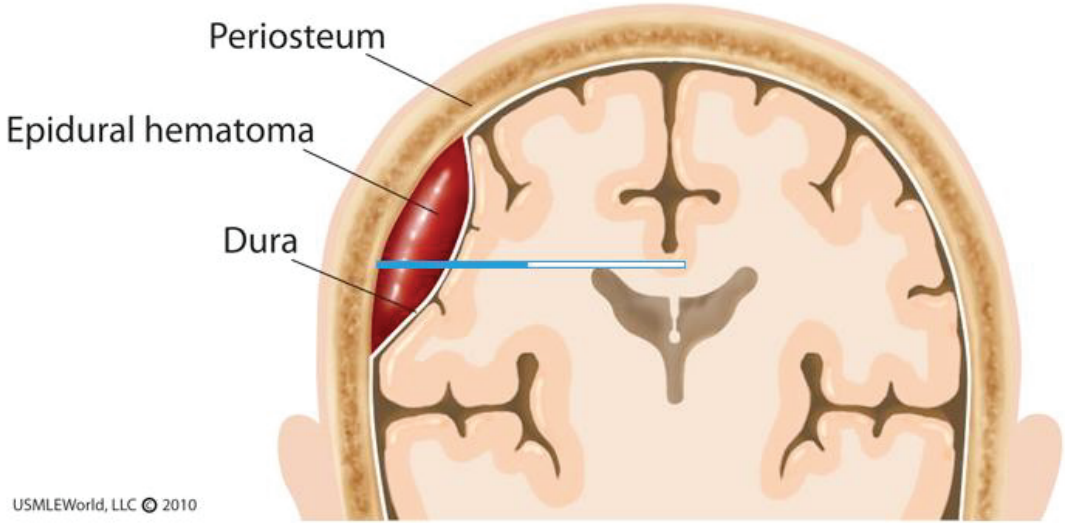


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[Choice D] The occipital artery arises opposite the facial artery from the external carotid, coursing



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**(Choice D)** The occipital artery arises opposite the facial artery from the external carotid, coursing posteriorly instead of anteriorly. This vessel supplies the posterior scalp and the sternocleidomastoid muscles.

**(Choice E)** The ophthalmic artery is the first branch of the internal carotid artery, supplying the eye and orbital contents as well as the eyelids, forehead, and nose. The internal carotid artery has no branches in the neck.

**(Choice F)** The sphenopalatine artery is a branch of the third part of the maxillary artery and supplies much of the nasal mucosa. It anastomoses with branches of the ophthalmic and facial arteries within the anterior part of the nasal septum in a region known as Kiesselbach's plexus (a frequent site of nosebleeds).

**Educational objective:**

The middle meningeal artery is a branch of the maxillary artery, which enters the skull at the foramen spinosum and courses intracranially deep to the pterion (where the frontal, parietal, temporal, and sphenoid bones meet). Skull fractures at this site may cause laceration of this vessel, leading to an epidural hematoma.

**References**

- Clinical importance of the middle meningeal artery.



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A 37-year-old man comes to the office due to difficulty sleeping. He says that his new job as a business executive is very stressful and requires considerable travel. During the past 3 months, the patient has made numerous trips between the United States and France. He experiences insomnia and daytime sleepiness for several days after these trips, but his sleep then improves significantly. Which of the following hypothalamic nuclei is most likely responsible for this delayed improvement in his symptoms?

- A. Anterior
- B. Lateral
- C. Posterior
- D. Suprachiasmatic
- E. Supraoptic
- F. Ventromedial

Submit



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A 37-year-old man comes to the office due to difficulty sleeping. He says that his new job as a business executive is very stressful and requires considerable travel. During the past 3 months, the patient has made numerous trips between the United States and France. He experiences insomnia and daytime sleepiness for several days after these trips, but his sleep then improves significantly. Which of the following hypothalamic nuclei is most likely responsible for this delayed improvement in his symptoms?

- A. Anterior (1%)
- B. Lateral (1%)
- C. Posterior (3%)
- ✓ D. Suprachiasmatic (83%)
- E. Supraoptic (6%)
- F. Ventromedial (4%)

Correct

83% Answered correctly

27 secs Time Spent

10/06/2020 Last Updated



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| Major functions of hypothalamic nuclei | |
|---|---|
| **Ventromedial** | Mediates satiety; destruction leads to hyperphagia |
| **Lateral** | Mediates hunger; destruction leads to anorexia |
| **Anterior** | Mediates heat dissipation; destruction leads to hyperthermia |
| **Posterior** | Mediates heat conservation; destruction leads to hypothermia |
| **Arcuate** | Secretion of dopamine (inhibits prolactin), GHRH |
| **Medial preoptic** | Secretion of GnRH, regulates sexual behavior |
| **Paraventricular** | Secretion of oxytocin, CRH, TRH & small amounts of ADH |
| **Supraoptic** | Secretion of ADH & small amounts of oxytocin |
| **Suprachiasmatic** | Circadian rhythm regulation & pineal gland function |

ADH = antidiuretic hormone; CRH = corticotropin-releasing hormone; GHRH = growth hormone-releasing hormone; GnRH = gonadotropin-releasing hormone; TRH = thyrotropin-releasing hormone.

This patient is experiencing **jet lag**, a syndrome associated with long flights that cross several time zones


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This patient is experiencing **jet lag**, a syndrome associated with long flights that cross several time zones. Symptoms include **insomnia**, **daytime drowsiness**, decreased work performance, gastrointestinal issues, and generalized malaise. Jet lag is caused by **dyssynchrony** between the body's circadian rhythms (eg, sleep/wake cycle) and the local environment (eg, daylight hours, sleep schedules).

Circadian rhythms are maintained by the **suprachiasmatic nucleus** (SCN). The SCN receives input from the retina and sends projections to other hypothalamic nuclei and the pineal gland. The primary functions of the SCN are to modulate body temperature and produce hormones such as cortisol (stress hormone) and **melatonin** (sleep-inducing hormone). Circulating melatonin levels are normally highest during the night and lowest during the day. In contrast, cortisol peaks in the morning and reaches its lowest level at night.

In patients with jet lag, the suprachiasmatic nucleus eventually **resynchronizes** the body clock to coincide with the environment over the course of several days. Eastward travel takes longer to recover from than westward travel because it is easier to lengthen the natural sleep/wake cycle than to shorten it. Treatment with **melatonin** supplementation can improve the symptoms of insomnia associated with jet lag.

**Educational objective:**
The suprachiasmatic nucleus regulates circadian rhythms by processing light information from the retina


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of the SCN are to modulate body temperature and produce hormones such as cortisol (stress hormone) and **melatonin** (sleep-inducing hormone). Circulating melatonin levels are normally highest during the night and lowest during the day. In contrast, cortisol peaks in the morning and reaches its lowest level at night.

In patients with jet lag, the suprachiasmatic nucleus eventually **resynchronizes** the body clock to coincide with the environment over the course of several days. Eastward travel takes longer to recover from than westward travel because it is easier to lengthen the natural sleep/wake cycle than to shorten it. Treatment with **melatonin** supplementation can improve the symptoms of insomnia associated with jet lag.

**Educational objective:**
The suprachiasmatic nucleus regulates circadian rhythms by processing light information from the retina and modulating body temperature and the production of hormones (eg, cortisol, melatonin). Dyssynchrony between the local environment (eg, daylight hours, sleep schedules) and internal circadian rhythms can cause insomnia and daytime sleepiness (ie, jet lag). Melatonin supplementation is recommended for the treatment of insomnia associated with jet lag.

| Physiology | Nervous System | Circadian rhythm |
| --- | --- | --- |
| Subject | System | Topic |


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A 59-year-old man comes to the emergency department with diplopia that started several hours ago. His past medical history is significant for long-standing diabetes with poor glycemic control, right-knee osteoarthritis, and peptic ulcer disease. Physical examination shows right-sided ptosis with the right pupil in the inferolateral position. Pupils are equal in size and reactive to light bilaterally. This patient's condition is most likely due to which of the following etiologies?

A. Nerve compression
B. Nerve inflammation
C. Nerve ischemia
D. Lacunar stroke
E. Muscle infiltration

Submit



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A 59-year-old man comes to the emergency department with diplopia that started several hours ago. His past medical history is significant for long-standing diabetes with poor glycemic control, right-knee osteoarthritis, and peptic ulcer disease. Physical examination shows right-sided ptosis with the right pupil in the inferolateral position. Pupils are equal in size and reactive to light bilaterally. This patient's condition is most likely due to which of the following etiologies?

- A. ~~Nerve compression~~ (21%)
- B. ~~Nerve inflammation~~ (11%)
- ✓ C. Nerve ischemia (54%)
- D. Lacunar stroke (9%)
- E. Muscle infiltration (2%)

Correct

54%
Answered correctly

01 min, 27 secs
Time Spent

03/12/2021
Last Updated



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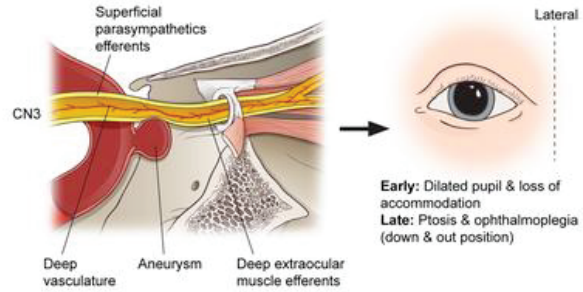
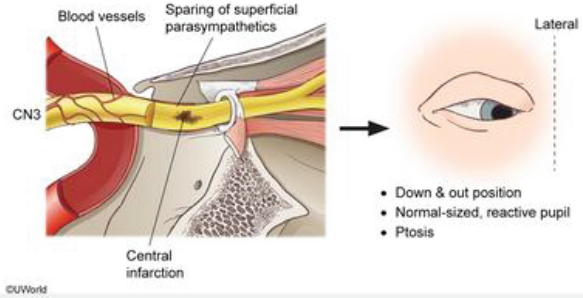
## Exhibit Display

### Aneurysmal compression of oculomotor nerve




### Diabetic ophthalmoplegia

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Neuropathy is a common chronic complication of diabetes mellitus. The clinical features of diabetic neuropathy vary considerably depending on the pattern of nerve involvement, which can be broadly divided into polyneuropathy, mononeuropathy, and autonomic neuropathy. Mononeuropathies can also be further subdivided into cranial and peripheral types.

All ocular motor nerves (III, IV, VI) can be affected in diabetes but unilateral cranial nerve III (CN III) involvement is most common. **Diabetic CN III mononeuropathy** classically presents with **acute onset diplopia**. On examination, the affected eye assumes a **"down and out" position** due to the unopposed pull by the superior oblique (CN IV) and lateral rectus (CN VI) muscles because all other extraocular muscles (inferior oblique and superior, inferior, and medial recti) are supplied by CN III. **Ptosis** also occurs due to paralysis of the levator palpebrae.

Diabetic mononeuropathy is caused by ischemic nerve damage, which predominantly involves the core of the CN III with relative sparing of the peripheral part. The somatic component of CN III that innervates the extraocular muscles is located centrally, but the autonomic component responsible for pupillary constriction and accommodation is located in the peripheral aspect of the nerve. Therefore, **pupillary size and reactivity is normal** in diabetic CN III mononeuropathy.



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**(Choice A)** CN III neuropathy can also occur due to nerve compression. Causes include transtentorial (uncal) herniation, neoplasms, and aneurysms of the posterior cerebral and posterior communicating arteries. In contrast to diabetic CN III mononeuropathy, pupillary dysfunction is often an early manifestation of external nerve compression due to injury of the peripherally located parasympathetic fibers.

**(Choices B and E)** Neither nerve inflammation nor muscle infiltration contributes to the development of diabetic neuropathy.

**(Choice D)** Lacunar midbrain strokes can involve the CN III nuclei. Because many neurologic pathways are densely packed in this area, CN III nuclei impairment is almost always associated with other neurologic deficits (eg, cerebellar ataxia, hemiparesis, or contralateral extrapyramidal symptoms). In addition, the contralateral superior rectus is affected because the subnucleus fibers decussate to the contralateral side. Midbrain lesions also cause bilateral ptosis because both levator palpebrae are innervated by a single subnucleus.

**Educational objective:**
Diabetic mononeuropathy often involves cranial nerve III. It is caused by predominantly central ischemia, which affects the somatic nerve fibers but spares peripheral parasympathetic fibers. Symptoms include ptosis, a "down and out" gaze, and normal light and accommodation reflexes.



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A 28-year-old woman, gravida 1 para 1, is seen in the clinic a week after spontaneous vaginal delivery. The delivery was performed under epidural analgesia and complicated by a prolonged second stage of labor. Since delivery, the patient has had frequent episodes of fecal incontinence, as well as mild perineal pain that is relieved by ibuprofen and opioid analgesics. She reports no other medical conditions, and her pregnancy was otherwise uncomplicated. On examination, a healing perineal laceration shows no signs of infection. Digital anorectal examination reveals decreased anal sphincter tone and loss of the anal wink reflex. Bilateral lower extremity reflexes are 2+ with normal tone. Which of the following is the most likely cause of this patient's fecal incontinence?

A. Cauda equina syndrome
B. Lumbosacral plexopathy
C. Opioid medication side effect
D. Pudendal nerve injury
E. Spinal epidural hematoma


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The delivery was performed under epidural analgesia and complicated by a prolonged second stage of labor. Since delivery, the patient has had frequent episodes of fecal incontinence, as well as mild perineal pain that is relieved by ibuprofen and opioid analgesics. She reports no other medical conditions, and her pregnancy was otherwise uncomplicated. On examination, a healing perineal laceration shows no signs of infection. Digital anorectal examination reveals decreased anal sphincter tone and loss of the anal wink reflex. Bilateral lower extremity reflexes are 2+ with normal tone. Which of the following is the most likely cause of this patient's fecal incontinence?

A. ~~Cauda equina syndrome~~ (8%)
B. Lumbosacral plexopathy (6%)
C. ~~Opioid medication side effect~~ (1%)
✓ D. Pudendal nerve injury (76%)
E. Spinal epidural hematoma (5%)

Correct

76%
Answered correctly

01 min
Time Spent

11/09/2020
Last Updated



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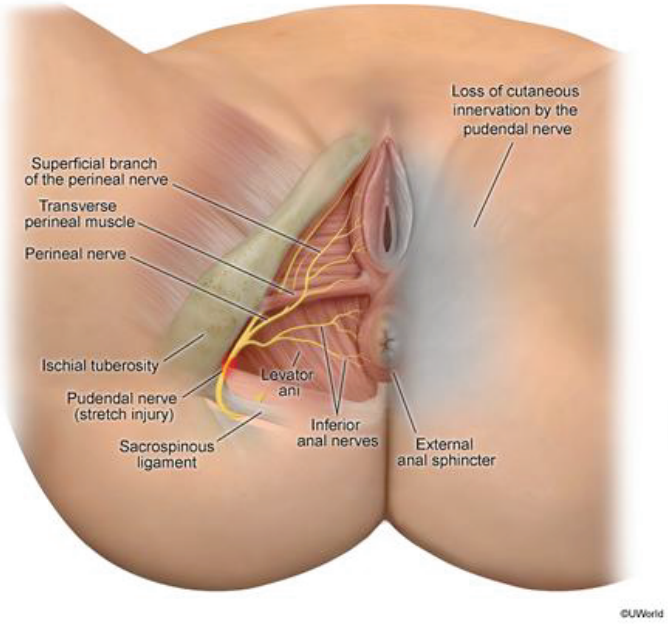
Exhibit Display

Pudendal nerve injury

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Inferior



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This postpartum patient has fecal incontinence consistent with **pudendal nerve injury**, which compromises motor and sensory innervation to the perineal region. The pudendal nerve originates from the ventral rami of S2-S4 and passes between the piriformis and coccygeus muscles as it exits the pelvis through the greater sciatic foramen. It then reenters the pelvis near the ischial spine through the lesser sciatic foramen before dividing into its terminal branches. Sensory branches innervate the external genitalia and skin around the anus and perineum. Motor branches innervate the **pelvic floor muscles** and **external urethral and anal sphincters**.

The pudendal nerve is vulnerable to **stretch injury** because of its curved course around the ischial spine. Labor and delivery (particularly active pushing during a **prolonged second stage** of labor) place excess tension on the pudendal nerve, increasing the likelihood of injury. Injury may result in denervation and weakness of the voluntary perineal musculature, including the external anal sphincter, which can present as new-onset **fecal incontinence** and **decreased anal sphincter tone** on digital anorectal examination. Because perianal skin sensation is compromised, patients also have **loss of the anal wink reflex**.

**(Choice A)** Cauda equina syndrome results from the compression of spinal nerve roots below the level of the conus medullaris. Patients present with severe unilateral or bilateral radicular pain, saddle anesthesia, and lower extremity weakness and hyporeflexia. Bowel and bladder incontinence are typically late


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**(Choice A)** Cauda equina syndrome results from the compression of spinal nerve roots below the level of the conus medullaris. Patients present with severe unilateral or bilateral radicular pain, saddle anesthesia, and lower extremity weakness and hyporeflexia. Bowel and bladder incontinence are typically late manifestations.

**(Choice B)** Lumbosacral plexopathy can occur due to direct compression of the lumbosacral trunk during fetal descent. Patients typically have transient footdrop and numbness of the lateral leg and dorsal foot.

**(Choice C)** An adverse effect of opioids is constipation, not fecal incontinence, due to decreased intestinal motility from the activation of gastrointestinal mu-opioid receptors. Opioids do not affect anal sphincter tone or the anal wink reflex.

**(Choice E)** Epidural hematoma is a rare complication of epidural analgesia that usually presents within hours to days, not weeks. Patients typically have sudden-onset back pain or radicular pain with progression to complete or partial paralysis of the lower extremities.

**Educational objective:**
Pudendal nerve injury can occur due to excessive stress on the pelvic floor during labor and delivery (eg, prolonged second stage). Nerve injury leads to denervation and weakness of the perineal musculature (eg, external anal sphincter), which can present as new-onset fecal incontinence.


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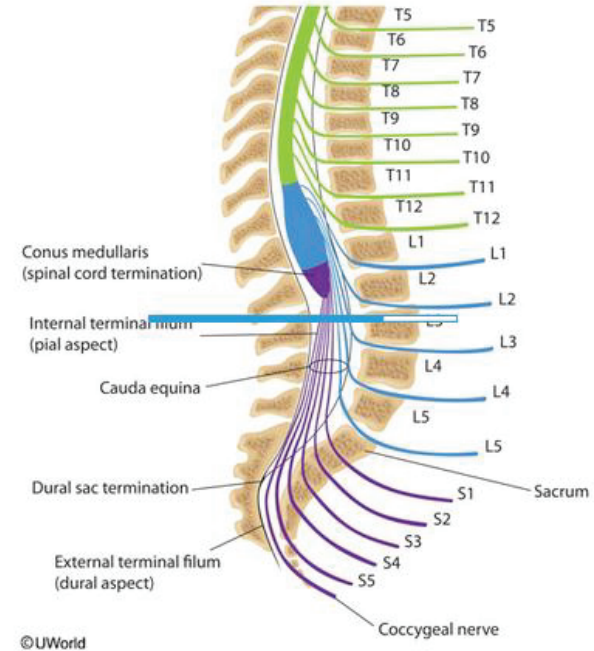
## Exhibit Display

**Relation of spinal nerve roots to vertebrae**

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external anal sphincter), which can present as new-onset fecal incontinence



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**(Choice B)** Lumbosacral plexopathy can occur due to direct compression of the lumbosacral trunk during fetal descent. Patients typically have transient footdrop and numbness of the lateral leg and dorsal foot.

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**(Choice E)** Epidural hematoma is a rare complication of epidural analgesia that usually presents within hours to days, not weeks. Patients typically have sudden-onset back pain or radicular pain with progression to complete or partial paralysis of the lower extremities.

**Educational objective:**

Pudendal nerve injury can occur due to excessive stress on the pelvic floor during labor and delivery (eg, prolonged second stage). Nerve injury leads to denervation and weakness of the perineal musculature (eg, external anal sphincter), which can present as new-onset fecal incontinence.

**References**

- Electrophysiological basis of fecal incontinence and its implications for treatment.

Anatomy Nervous System Fecal incontinence



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Electric stimulation of the musculocutaneous nerve causes a rapid twitch of the biceps muscle. Electron microscopy shows numerous vesicles within the musculocutaneous nerve terminals. In order for these vesicles to release their contents into the synaptic cleft, which of the following substances is required?

- A. Sodium
- B. Calcium
- C. cAMP
- D. IP3
- E. DAG
- F. cGMP

Submit



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Electric stimulation of the musculocutaneous nerve causes a rapid twitch of the biceps muscle. Electron microscopy shows numerous vesicles within the musculocutaneous nerve terminals. In order for these vesicles to release their contents into the synaptic cleft, which of the following substances is required?

- A. Sodium (3%)
- ✓ B. Calcium (89%)
- C. cAMP (3%)
- D. IP3 (2%)
- E. DAG (0%)
- F. cGMP (0%)

Correct

89% Answered correctly

23 secs Time Spent

01/30/2021 Last Updated



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The synaptic vesicles in motor neuron presynaptic terminals contain acetylcholine (ACh). When an action potential depolarizes the presynaptic terminal membrane, voltage-gated calcium channels open, causing an influx of extracellular calcium into the synaptic terminal. This calcium current stimulates fusion of the presynaptic vesicles with the plasma membrane and exocytosis of ACh. The nicotinic ACh receptors on the postsynaptic skeletal muscle end plate are ligand-gated sodium and potassium ion channels. The increased sodium and potassium conductance that occurs with ACh binding generates a motor end plate potential that signals for depolarization of the muscle cell membrane. ACh in the synaptic cleft is degraded by acetylcholinesterase.

**(Choice A)** Rapid sodium influx is responsible for the upstroke of the action potential in skeletal muscle, smooth muscle, cardiac muscle and Purkinje fibers. In contrast, the initial upstroke of the action potential in the SA node depends on calcium influx.

**(Choices C- F)** Second messengers do not play a role in the release of synaptic vesicle contents (ACh) at the neuromuscular junction.

**Educational Objective:**
Acetylcholine release from presynaptic terminal vesicles at the neuromuscular junction depends upon the


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presynaptic vesicles with the plasma membrane and exocytosis of ACh. The nicotinic ACh receptors on the postsynaptic skeletal muscle end plate are ligand-gated sodium and potassium ion channels. The increased sodium and potassium conductance that occurs with ACh binding generates a motor end plate potential that signals for depolarization of the muscle cell membrane. ACh in the synaptic cleft is degraded by acetylcholinesterase.

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**(Choices C- F)** Second messengers do not play a role in the release of synaptic vesicle contents (ACh) at the neuromuscular junction.

**Educational Objective:**
Acetylcholine release from presynaptic terminal vesicles at the neuromuscular junction depends upon the influx of extracellular calcium into the presynaptic terminal. Calcium influx into the nerve terminal occurs following neuronal depolarization and opening of voltage-gated calcium channels.

| Pathophysiology | Nervous System | Neuromuscular junction |
|---|---|---|
| Subject | System | Topic |


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A 63-year-old man comes to the physician's office due to long-standing osteoarthritis that is refractory to over-the-counter analgesics. After discussing various treatment options with his physician, the patient is referred to a surgeon for right total hip arthroplasty. His acute postoperative course is unremarkable. During a follow-up appointment, the patient reports difficulty walking despite minimal pain. On examination, he leans to his right side when walking. When asked to stand on his right leg, the patient's left hip tilts downward. Which of the following nerves is most likely injured in this patient?

A. Femoral
B. Inferior gluteal
C. Obturator
D. Sciatic
E. Superior gluteal

Submit



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A 63-year-old man comes to the physician's office due to long-standing osteoarthritis that is refractory to over-the-counter analgesics. After discussing various treatment options with his physician, the patient is referred to a surgeon for right total hip arthroplasty. His acute postoperative course is unremarkable. During a follow-up appointment, the patient reports difficulty walking despite minimal pain. On examination, he leans to his right side when walking. When asked to stand on his right leg, the patient's left hip tilts downward. Which of the following nerves is most likely injured in this patient?

A. Femoral (1%)
B. Inferior gluteal (18%)
C. Obturator (6%)
D. Sciatic (2%)
✓ E. Superior gluteal (70%)

Correct

70% Answered correctly

45 secs Time Spent

10/18/2020 Last Updated



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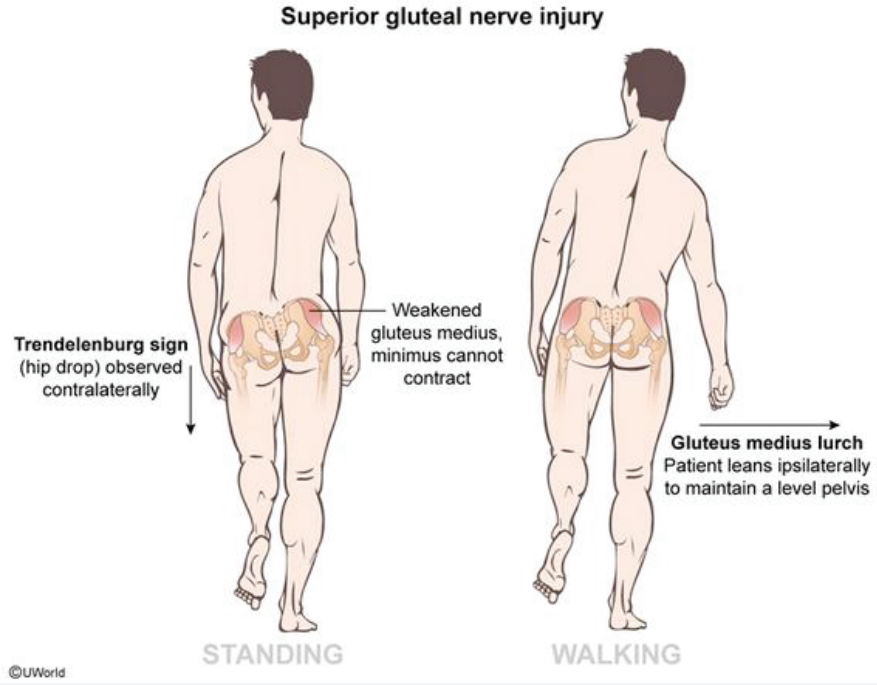


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This patient has **superior gluteal nerve** injury, which is most often caused by pelvic trauma or iatrogenic damage occurring during hip surgery or buttocks injections. The superior gluteal nerve innervates the gluteus medius, gluteus minimus, and tensor fasciae latae muscles. These muscles function to **stabilize the pelvis** and **abduct the thigh**. **Weakness** of the gluteus medius and gluteus minimus muscles will cause the **pelvis** to **sag toward** the **unaffected (contralateral) side** when the **patient stands** on the affected leg (positive Trendelenburg sign). When **walking**, the patient will **lean toward** the **affected (ipsilateral) side** to compensate for the hip drop (gluteus medius lurch).

**(Choice A)** The femoral nerve innervates the muscles responsible for flexion of the thigh at the hip (eg, iliacus and sartorius muscles) and extension of the leg at the knee (eg, quadriceps femoris). It also supplies sensory innervation to the skin on the anterior thigh and medial leg. Injury results in knee buckling and loss of the patellar reflex.

**(Choice B)** The inferior gluteal nerve innervates the gluteus maximus muscle, which is responsible for extension and external rotation of the thigh at the hip. Inferior gluteal nerve injury typically causes difficulty in rising from a seated position and climbing stairs.

**(Choice C)** Injury of the obturator nerve causes impaired thigh adduction and medial thigh sensory loss.


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**(Choice B)** The inferior gluteal nerve innervates the gluteus maximus muscle, which is responsible for extension and external rotation of the thigh at the hip. Inferior gluteal nerve injury typically causes difficulty in rising from a seated position and climbing stairs.

**(Choice C)** Injury of the obturator nerve causes impaired thigh adduction and medial thigh sensory loss.

**(Choice D)** The sciatic nerve innervates the muscles in the posterior compartment of the thigh (ie, hamstrings). It subsequently divides into the tibial and common fibular/common peroneal nerves, which provide motor and sensory innervation to the leg and foot.

**Educational objective:**
Superior gluteal nerve injury results in weakness and paralysis of the gluteus medius, gluteus minimus, and tensor fasciae latae muscles. This causes the pelvis to tilt downward toward the contralateral side (positive Trendelenburg sign). Patients will also lean toward the ipsilateral side when walking to help stabilize the pelvis (gluteus medius gait).

| Anatomy | Nervous System | Falls |
|---|---|---|
| Subject | System | Topic |

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An 82-year-old man is found unresponsive by his neighbor. The patient lives alone in his suburban home. When the neighbor went to check on him, the patient was on the floor and not answering any questions. His medical history is unknown. On arrival of emergency medical services, the patient is obtunded and responds only to painful stimuli. Supportive measures are begun, including endotracheal intubation, but the patient dies en route to the hospital. Autopsy reveals extensive atherosclerotic disease involving the coronary and internal carotid arteries. Histopathologic examination of the brain in the right middle cerebral artery territory shows neurons with intensely eosinophilic cytoplasm and nuclear fragmentation. Based on these findings, this patient's cerebral injury most likely occurred approximately how long ago?

A. Less than an hour
B. 12-24 hours
C. 1-2 weeks
D. 2 months
E. 2 years



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When the neighbor went to check on him, the patient was on the floor and not answering any questions. His medical history is unknown. On arrival of emergency medical services, the patient is obtunded and responds only to painful stimuli. Supportive measures are begun, including endotracheal intubation, but the patient dies en route to the hospital. Autopsy reveals extensive atherosclerotic disease involving the coronary and internal carotid arteries. Histopathologic examination of the brain in the right middle cerebral artery territory shows neurons with intensely eosinophilic cytoplasm and nuclear fragmentation. Based on these findings, this patient's cerebral injury most likely occurred approximately how long ago?

A. ~~Less than an hour~~ (12%)
✓ B. 12-24 hours (82%)
C. 1-2 weeks (4%)
D. 2 months (0%)
E. 2 years (0%)

Correct

82%

01 min, 06 secs

01/01/2021



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| Ischemic stroke | | |
|---|---|---|
| **Time after injury** | **Microscopic changes** | **Macroscopic changes** |
| 12-24 hours | Red neurons (eosinophilic cytoplasm, pyknotic nuclei, loss of Nissl substance) | |
| 24-72 hours | Neutrophilic infiltration | |
| 3-7 days | Macrophage/microglia infiltration & phagocytosis begins | |
| 1-2 weeks | Reactive gliosis & vascular proliferation around the necrotic area | Liquefactive necrosis (1 week-1 month) |
| >2 weeks | Glial scar formation | Cystic area surrounded by dense glial fibers (>1 month) |

This patient was found unconscious, in rapid hemodynamic decline, an unknown amount of time after an inciting cardiovascular event. The autopsy demonstrates histopathologic evidence of **ischemic stroke**


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| | | |
|---|---|---|
| | | glial fibers (> 1 month) |

This patient was found unconscious, in rapid hemodynamic decline, an unknown amount of time after an inciting cardiovascular event. The autopsy demonstrates histopathologic evidence of **ischemic stroke** caused by widespread atherosclerosis. Sustained interruption in blood circulation to branches of the internal carotid arteries (eg, middle cerebral artery) can lead to tissue hypoxia and **irreversible cellular injury** with characteristic microscopic and macroscopic changes.

Specific findings vary with time but follow a predictable course. **Red neurons** are typically seen **12-24 hours** after irreversible ischemic injury and are characterized by intense **eosinophilic staining** of the cytoplasm due to dissolution of **Nissl bodies** (basophilic granules consisting of rough endoplasmic reticulum and ribosomes). The nuclei also become pyknotic (eg, shrunken and deeply basophilic) and undergo **fragmentation** (karyorrhexis). After about a day, the tissue damage promotes neutrophil infiltration, followed by macrophage/microglial recruitment a few days later.

**(Choice A)** There is typically little change in the microscopic or macroscopic appearance of brain tissue <1 hour after irreversible ischemic injury.

**(Choice C)** At 1-2 weeks, there will be robust phagocytosis of neuron and myelin breakdown products by activated macrophages/microglia. Around this time, astrocytes start proliferating with the development of a


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**(Choice A)** There is typically little change in the microscopic or macroscopic appearance of brain tissue <1 hour after irreversible ischemic injury.

**(Choice C)** At 1-2 weeks, there will be robust phagocytosis of neuron and myelin breakdown products by activated macrophages/microglia. Around this time, astrocytes start proliferating with the development of a network of cytoplasmic extensions (reactive gliosis), and new vessels are formed in the periphery of the necrotic area.

**(Choices D and E)** Several months to years after brain infarction, the necrotic area appears as a cystic cavity surrounded by a wall of dense fibers formed by astrocytic processes (glial scar).

**Educational objective:**

Inadequate blood supply to the brain (eg, arterial thrombosis or embolism) leads to ischemic stroke. The first microscopic changes are typically seen 12-24 hours after irreversible ischemic injury and include intense eosinophilic staining of the neuronal cytoplasm (red neurons) and nuclear fragmentation.

**References**

- Histopathological changes in acute ischemic stroke.

Pathology Nervous System Ischemic stroke



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A 32-year-old woman describes five episodes of intractable vomiting over the last year. The episodes last several hours and are associated with a sensation that the room is spinning or tilting. At these times, it is difficult for her to walk because she loses her balance. She cannot relate the timing of the episodes to any particular inciting event. Physical examination reveals stability in the Romberg position and during tandem walk. Proprioception is intact. Dysfunction of which of the following structures best explains this patient's symptoms?

A. Posterior columns of the spinal cord
B. Vagal nerve
C. Optic tract
D. Inner ear
E. Cerebellum
F. Frontal cortex

Submit



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A. ~~Posterior columns of the spinal cord~~ (0%)
B. Vagal nerve (2%)
C. ~~Optic tract~~ (0%)
D. Inner ear (90%)
E. Cerebellum (5%)
F. Frontal cortex (0%)


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This patient is experiencing vertigo due to vestibular dysfunction. Vertigo is a sensation of motion when no motion is present or an exaggerated sense of motion for a given bodily movement. It must be distinguished from other sensations that are often described by patients using similar terminology, such as imbalance, light-headedness, and syncope. Vertigo resulting from vestibular dysfunction tends to be of sudden onset, interfere with walking, and cause nausea and vomiting. Typical causes of vestibulopathy include Meniere's disease, perilymphatic fistulas, benign positional vertigo, labyrinthitis, and acoustic neuromas.

**(Choice A)** Disease of the posterior column of the spinal cord can occur in syphilis (i.e., tabes dorsalis) and vitamin B12 deficiency. Typical symptoms include ataxia, decreased proprioception and vibratory sense, and hyporeflexia. This patient's normal neurologic exam makes posterior column disease unlikely.

**(Choice B)** Vagal nerve damage can present as hoarseness, dysphagia, abnormal gastrointestinal motility, or tachycardia. Vagal nerve dysfunction will not cause vertigo.

**(Choice C)** Optic tract dysfunction will result in visual problems. Vision deficits do not typically cause vertigo, but may cause people to feel unsteady on their feet.

**(Choice E)** Cerebellar dysfunction presents as ataxia, imbalance, incoordination, and nystagmus. Patients with cerebellar dysfunction will be unable to perform tandem walking due to their imbalance



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**(Choice B)** Vagal nerve damage can present as hoarseness, dysphagia, abnormal gastrointestinal motility, or tachycardia. Vagal nerve dysfunction will not cause vertigo.

**(Choice C)** Optic tract dysfunction will result in visual problems. Vision deficits do not typically cause vertigo, but may cause people to feel unsteady on their feet.

**(Choice E)** Cerebellar dysfunction presents as ataxia, imbalance, incoordination, and nystagmus. Patients with cerebellar dysfunction will be unable to perform tandem walking due to their imbalance.

**(Choice F)** The frontal cortex controls executive functions and response inhibition. Damage to the frontal cortex results in "frontal release" symptoms, such as personality change, inability to organize or plan, and disinhibition.

**Educational Objective:**
Vertigo is a sensation of excessive motion compared to physical reality. It is most commonly due to dysfunction within the vestibular system.

| Pathology | Nervous System | Vertigo |
|---|---|---|
| Subject | System | Topic |


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A 27-year-old woman comes to the office due to severe, unilateral, throbbing headaches that occur several times a month. The headaches are associated with photophobia, nausea, and occasional vomiting. Over-the-counter analgesics do not provide significant symptom relief. Her mother has a history of similar headaches. Vital signs are within normal limits. Physical examination reveals no abnormalities. A medication is prescribed to treat her condition and the patient is instructed to take it immediately at the onset of a headache. This medication most likely decreases the severity and duration of this patient's headache through which of the following mechanisms?

A. Blockade of dopamine receptors in mesolimbic tract
B. Blockade of serotonin reuptake in cortico-amygdala circuitry
C. Increased availability of acetylcholine in cortical synapses
D. Stimulation of periaqueductal gray area mu receptors
E. Stimulation of trigeminovascular serotonin receptors

Submit



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A. ~~Blockade of dopamine receptors in mesolimbic tract~~ (4%)

B. Blockade of serotonin reuptake in cortico-amygdala circuitry (16%)

C. ~~Increased availability of acetylcholine in cortical synapses~~ (2%)

D. Stimulation of periaqueductal gray area mu receptors (5%)

✓ E. Stimulation of trigeminovascular serotonin receptors (71%)

71%  01 min, 10 secs  09/20/2020



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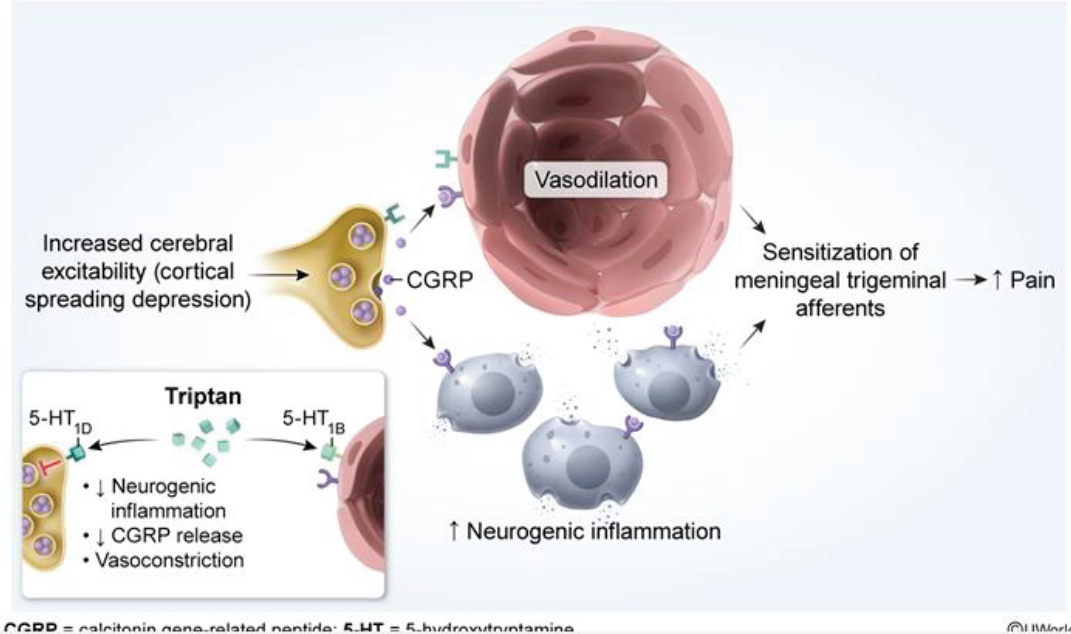
## Migraine pathogenesis & triptan mechanism of action




CGRP = calcitonin gene-related peptide; 5-HT = 5-hydroxytryptamine

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CGRP = calcitonin gene-related peptide; 5-HT = 5-hydroxytryptamine. ©UWorld

**Migraines** are recurrent, debilitating, unilateral headaches with a pulsating or throbbing quality lasting between 4-72 hours, often with photophobia, phonophobia, and nausea. They can be associated with an aura and are more common in younger women.

Although the pathogenesis of migraines is multifactorial and not fully understood, it is associated with cortical spreading depression (ie, self-propagating neurotransmission across the cortex). Subsequent stimulation of **trigeminal afferents** in the meninges causes the release of **vasoactive neuropeptides**, including substance P and **calcitonin gene–related peptide** (CGRP), leading to neurogenic inflammation, vasodilation, and plasma protein extravasation. These substances may also contribute to the increased sensitivity of nociceptive pathways to stimuli (ie, neuronal sensitization).

**Triptans** (eg, sumatriptan) are serotonin **5-hydroxytryptamine 1B/1D agonists** that directly counter migraine headaches by binding to trigeminal serotonin receptors and **inhibiting CGRP** release from the trigeminal neurons. In addition, triptans bind serotonin receptors on the smooth muscle cells of blood vessels, resulting in intracranial vasoconstriction. Triptans are commonly prescribed as **abortive therapy** for acute migraines, particularly in patients who are not responsive to analgesics. Significant adverse effects include dizziness, chest tightness, and **hypertension**.



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effects include dizziness, chest tightness, and **hypertension**.

**(Choice A)** Antipsychotic medications (eg, haloperidol, risperidone) block the dopamine receptors in the mesolimbic tract and are used in schizophrenia or bipolar disorder. They are not indicated in the treatment of migraine.

**(Choice B)** Selective serotonin reuptake inhibitors (eg, sertraline, citalopram) block serotonin reuptake in cortico-amygdala pathways. These drugs are used to treat depression and anxiety, not to abort migraines.

**(Choice C)** Acetylcholinesterase inhibitors (eg, rivastigmine, galantamine) increase the availability of acetylcholine at cortical synapses and are indicated in the treatment of dementia (eg, Alzheimer disease).

**(Choice D)** Opioid medications (eg, morphine, oxycodone) stimulate mu receptors in the periaqueductal gray area, resulting in modulation of pain. Opioids are not indicated in the treatment of migraines because they increase the risk of chronic migraine, carry a risk of dependence, and are less effective than triptans.

**Educational objective:**
The pathogenesis of migraines is complex and multifactorial but includes neurogenic inflammation, vasodilation, and sensitization of trigeminal afferents in the meninges. Triptans are serotonin 5-hydroxytryptamine 1B/1D agonists that stimulate the trigeminovascular serotonin receptors, resulting in inhibition of vasoactive peptide release, intracranial vasoconstriction, and decreased pain. They are used



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mesolimbic tract and are used in schizophrenia or bipolar disorder. They are not indicated in the treatment of migraine.

**(Choice B)** Selective serotonin reuptake inhibitors (eg, sertraline, citalopram) block serotonin reuptake in cortico-amygdala pathways. These drugs are used to treat depression and anxiety, not to abort migraines.

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The pathogenesis of migraines is complex and multifactorial but includes neurogenic inflammation, vasodilation, and sensitization of trigeminal afferents in the meninges. Triptans are serotonin 5-hydroxytryptamine 1B/1D agonists that stimulate the trigeminovascular serotonin receptors, resulting in inhibition of vasoactive peptide release, intracranial vasoconstriction, and decreased pain. They are used as abortive therapy for acute migraine.

**References**


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A 16-year-old boy is brought to the emergency department after an eye injury during a baseball game. He was batting for his high school team when the opposing pitcher made a wild throw and the baseball hit him in the right eye. The patient has since been having diplopia that worsens when he looks up. On physical examination, he has mild periorbital ecchymosis, enophthalmos, and limited vertical movement of the right eye. Visual acuity and left eye examination are normal. CT scan of the head reveals an orbital floor fracture. Which of the following additional findings is most likely to be seen in this patient?

A. Absent right corneal reflex
B. Bruising over the mastoid process
C. Impaired olfaction
D. Inability to puff out right cheek
E. Reduced sensation over right upper lip

Submit



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A 16-year-old boy is brought to the emergency department after an eye injury during a baseball game. He was batting for his high school team when the opposing pitcher made a wild throw and the baseball hit him in the right eye. The patient has since been having diplopia that worsens when he looks up. On physical examination, he has mild periorbital ecchymosis, enophthalmos, and limited vertical movement of the right eye. Visual acuity and left eye examination are normal. CT scan of the head reveals an orbital floor fracture. Which of the following additional findings is most likely to be seen in this patient?

A. ~~Absent right corneal reflex~~ (27%)
B. Bruising over the mastoid process (10%)
C. ~~Impaired olfaction~~ (11%)
D. Inability to puff out right cheek (9%)
E. Reduced sensation over right upper lip (41%)

Incorrect
Correct answer
E

41%
Answered correctly

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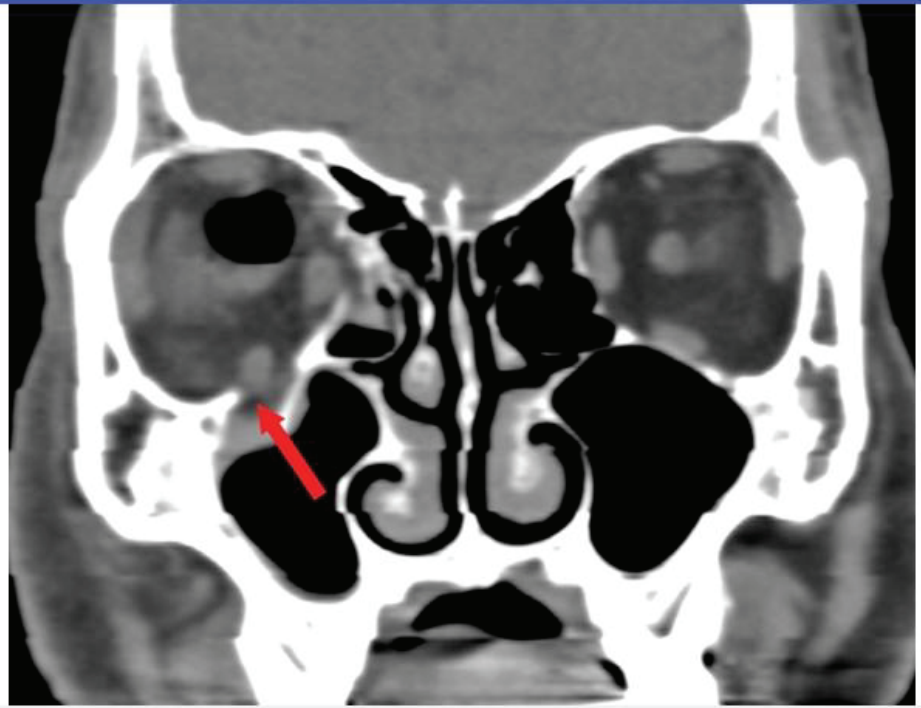

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Fractures to the **orbital floor**, which is composed of the zygomatic bone and maxilla, most commonly result from direct frontal trauma to the orbit due to assault, motor vehicle crashes, or sports injuries. The **infraorbital nerve** (continuation of the maxillary nerve) runs along the orbital surface of the maxilla in the infraorbital groove before traversing the infraorbital canal and exiting the skull via the infraorbital foramen (just below the orbit). Damage can result in numbness and paresthesia of the **upper cheek, upper lip**, and **upper gingiva**. In addition, displacement of the orbital contents through the floor may cause enophthalmos, and entrapment of the inferior rectus muscle (as seen in above CT) can impair vertical gaze.

**(Choice A)** The corneal reflex involves cranial nerves $V_1$ (sensory) and VII (motor) and processing in the pons. It can be impaired by trauma to the superior orbital fissure because cranial nerves III, IV, V, and VI pass through this structure.

**(Choice B)** Hematomas over the mastoid process (Battle sign), along with periorbital ecchymosis and clear otorrhea, are signs of basilar skull fractures.

**(Choice C)** Nasal fractures or high force trauma to the midface can result in loss of smell if the olfactory nerves are torn from the cribriform plate in the ethmoid bone.


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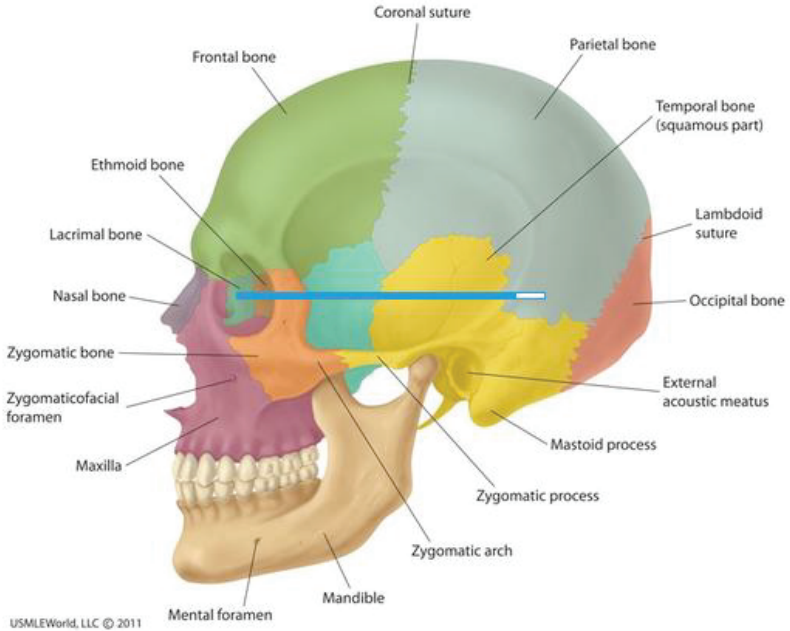
Exhibit Display

Skull, lateral view

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## Exhibit Display

**Mastoid or periauricular hematomas (Battle sign)**

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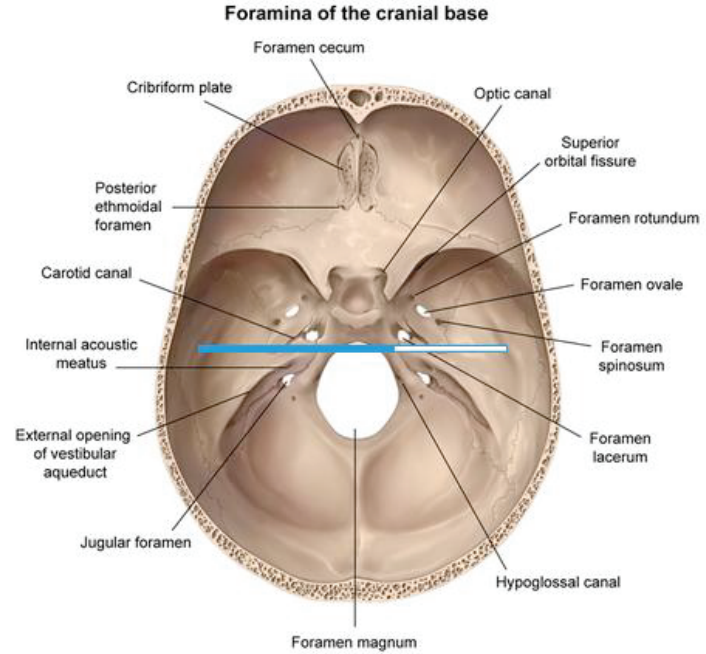


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pons. It can be impaired by trauma to the superior orbital fissure because cranial nerves III, IV, V, and VI pass through this structure.

**(Choice B)** Hematomas over the mastoid process (Battle sign), along with periorbital ecchymosis and clear otorrhea, are signs of basilar skull fractures.

**(Choice C)** Nasal fractures or high force trauma to the midface can result in loss of smell if the olfactory nerves are torn from the cribriform plate in the ethmoid bone.

**(Choice D)** The facial nerve (cranial nerve VII) controls the motor function of the face and can be impaired in fractures of the temporal bone after lateral head trauma or zygomatic orbit fractures.

**Educational objective:**

Fractures to the orbital floor commonly result from direct frontal trauma to the orbit. The infraorbital nerve runs along the orbital floor in a groove in the maxilla before exiting the skull just inferior to the orbit. Damage can result in paresthesia of the upper cheek, upper lip, and upper gingiva. In addition, the inferior rectus muscle can also become entrapped, limiting vertical gaze.

**References**

- Orbital fractures: a review.
- Pediatric orbital fractures.



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www.ncbi.nlm.nih.gov/pubmed/21339801

An 11-year-old boy is brought to the emergency department by ambulance after he briefly lost consciousness. The patient's mother found him on the kitchen floor shaking and jerking. She believes that he was out of her sight for only a few minutes. When asked about any other abnormal behaviors, she says that her son often stares into space and does not respond to questions during these episodes. The patient has no known medical conditions or history of recent illnesses. He is afebrile with normal vital signs. The patient seems sleepy but is oriented to time and place and has no abnormalities on physical examination. Several hours later, he is alert and says that he wants to go home. Which of the following agents is the best long-term treatment for this patient?

A. Carbamazepine
B. Ethosuximide
C. Gabapentin
D. Phenytoin
E. Valproic acid



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A. Carbamazepine (4%)
B. Ethosuximide (46%)
C. Gabapentin (0%)
D. Phenytoin (4%)
E. Valproic acid (43%)

Correct

43%

51 secs

02/27/2021



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| Seizure type | Description | Preferred anticonvulsants |
|---|---|---|
| **Focal onset** (involves a single cerebral hemisphere at onset) | | |
| **Aware** | • No loss of consciousness or postictal state<br>• Motor, sensory, autonomic, or cognitive symptoms | • Carbamazepine*<br>• Lamotrigine<br>• Levetiracetam<br>• Phenytoin* |
| **Impaired awareness** | • Appears awake but consciousness is altered (eg, blank stare)<br>• Postictal state<br>• May have automatisms (eg, lip smacking) | |
| **Generalized onset** (involves both hemispheres at onset) | | |
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state | |



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| | | |
|---|---|---|
| | followed by rhythmic jerking (clonic) | • Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |
| **Absence** | • Brief episodes of altered consciousness (eg, blank stare)<br>• May have automatisms<br>• Usually no postictal state | • Ethosuxamide<br>• Valproic acid |

*Narrow-spectrum agents can also treat focal-onset seizures that evolve into bilateral tonic-clonic seizures.

This patient with frequent staring spells (ie, **absence seizures**) and an unprovoked **tonic-clonic seizure** most likely has undiagnosed juvenile absence epilepsy. Absence seizures are characterized by momentary lapses in consciousness (~10 seconds) associated with a classic 3-Hz spike-wave pattern on electroencephalogram. Younger children with absence seizures typically do not develop other seizure types; however, later onset (eg, age 10-12) of absence epilepsy is associated with an increased incidence of generalized onset tonic-clonic or myoclonic seizures.

Although a first-time unprovoked seizure may not require treatment, this patient has had multiple seizures,


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of generalized onset tonic-clonic or myoclonic seizures.

Although a first-time unprovoked seizure may not require treatment, this patient has had multiple seizures, including both absence and tonic-clonic seizures. Ethosuximide is the preferred first-line agent for the treatment of isolated absence seizures; however, it does not suppress tonic-clonic seizures **(Choice B)**. Treatment with a **broad-spectrum** antiepileptic such as **valproic acid** is required in these patients because it is effective for both absence and tonic-clonic seizures.

**(Choices A, C, and D)** Carbamazepine, phenytoin, and gabapentin are narrow-spectrum antiepileptics that can be used to treat focal onset seizures (including focal onset seizures that progress to bilateral tonic-clonic seizures). However, they are not effective for treating generalized onset seizures (eg, absence, myoclonic) which can actually be worsened by treatment with carbamazepine or phenytoin.

**Educational objective:**
Older children with absence seizures may also develop generalized onset tonic-clonic or myoclonic seizures. Although ethosuximide is effective against isolated absence seizures, it is not effective for tonic-clonic seizures. Valproic acid is a broad-spectrum antiepileptic that treats both types of seizures.

**References**

- Ethosuximide, sodium valproate or lamotrigine for absence seizures in children and adolescents.



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A 42-year-old previously healthy man comes to the office due to an enlarging mole. The patient has had a mole on his forearm for the past several years, and it has rapidly increased in size over the past 4 months. Physical examination shows an 8-mm raised lesion with variegated pigmentation and ill-defined borders on the right forearm. Excisional biopsy of the lesion is planned. Local anesthesia is administered via an infiltrating injection of lidocaine mixed with epinephrine. Which of the following is the most likely impact of mixing the latter medication with the anesthetic agent?

A. Altered neurotransmitter levels of nociceptive fibers
B. Decreased pain during subcutaneous infiltration
C. Increased anesthesia efficacy by synergistic effect
D. Increased anesthesia potency by decreasing tissue pH
E. Prolonged duration of action of the anesthetic agent

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A. ~~Altered neurotransmitter levels of nociceptive fibers~~ (4%)
B. ~~Decreased pain during subcutaneous infiltration~~ (4%)
C. ~~Increased anesthesia efficacy by synergistic effect~~ (22%)
D. ~~Increased anesthesia potency by decreasing tissue pH~~ (5%)
✓ E. Prolonged duration of action of the anesthetic agent (63%)

Correct

63%
Answered correctly

58 secs
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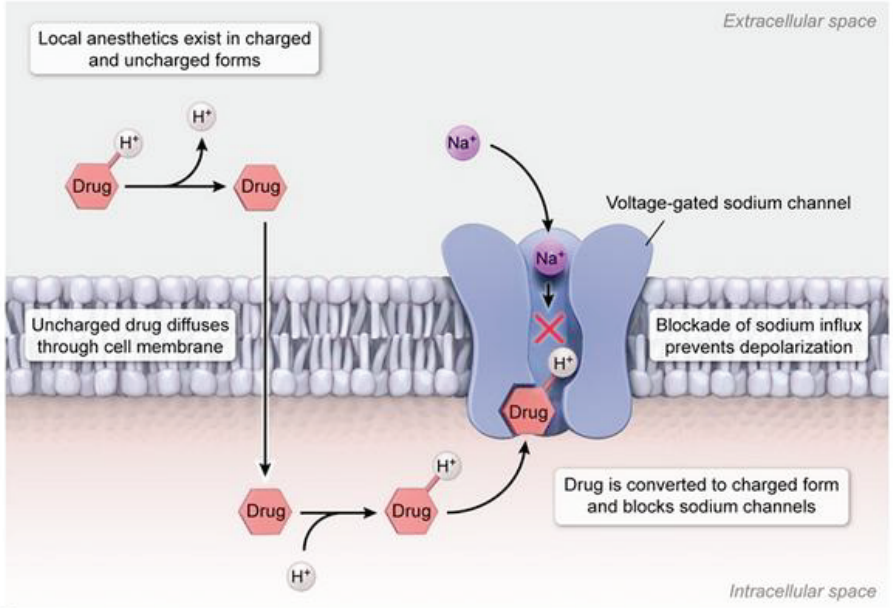
## Local anesthetic mechanism of action

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Lidocaine is a **local anesthetic** that blocks transmission from free nerve endings. It is often mixed with epinephrine, which causes **profound vasoconstriction** when injected subcutaneously. This results in the following:

- A decrease in local bleeding, making the procedure easier to complete
- **A prolonged duration of action** because more lidocaine remains at the site of injection
- A decrease in systemic absorption, reducing the potential for serious adverse effects (eg, arrhythmias, seizures)

**(Choice A)** Although epinephrine acts as a catecholamine neurotransmitter in the CNS, it mediates autonomic functions in the peripheral nervous system. Glutamate and substance P are the main neurotransmitters of pain sensation in the peripheral nervous system.

**(Choices B and D)** Local anesthetics are weak bases that exist in charged and uncharged forms; the uncharged form must diffuse through the cell membrane and bind the inside portion of sodium channels in order to prevent depolarization. Increased acidity in the surrounding tissue results in more anesthetic molecules remaining in the charged form, preventing them from penetrating the cell membrane to exert an effect. Therefore, sodium bicarbonate is often added to lidocaine with epinephrine to increase the pH, which improves potency. This increase in pH also decreases pain at the injection site.



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**(Choices B and D)** Local anesthetics are weak bases that exist in charged and uncharged forms; the uncharged form must diffuse through the cell membrane and bind the inside portion of sodium channels in order to prevent depolarization. Increased acidity in the surrounding tissue results in more anesthetic molecules remaining in the charged form, preventing them from penetrating the cell membrane to exert an effect. Therefore, sodium bicarbonate is often added to lidocaine with epinephrine to increase the pH, which improves potency. This increase in pH also decreases pain at the injection site.

**(Choice C)** Medications interact synergistically when they produce the same result by different mechanisms (eg, opioids + acetaminophen). Epinephrine does not produce anesthesia, so although it prolongs the duration of anesthesia, it does not act synergistically to increase the anesthetic effect.

**Educational objective:**
Epinephrine is often added to lidocaine to produce vasoconstriction, which prolongs lidocaine's duration of action, decreases bleeding during the procedure, and reduces systemic lidocaine absorption.

| Pharmacology | Nervous System | Anesthesia |
|---|---|---|
| Subject | System | Topic |

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A 54-year-old man comes to the physician with recent-onset mild headaches and left leg weakness. The lesions seen on physical examination are shown in the image below.

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Which of the following inheritance patterns is this patient's disorder most likely to exhibit?

- A. Genomic imprinting
- B. Mitochondrial
- C. Multifactorial
- D. Single-gene autosomal dominant
- E. Single-gene autosomal recessive
- F. Single-gene X-linked

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Which of the following inheritance patterns is this patient's disorder most likely to exhibit?

A. ~~Genomic imprinting~~ (0%)

B. ~~Mitochondrial~~ (1%)

C. Multifactorial (5%)

D. Single-gene autosomal dominant (71%)

E. Single-gene autosomal recessive (17%)

F. Single-gene X-linked (3%)

Incorrect

71%

40 secs

10/21/2020



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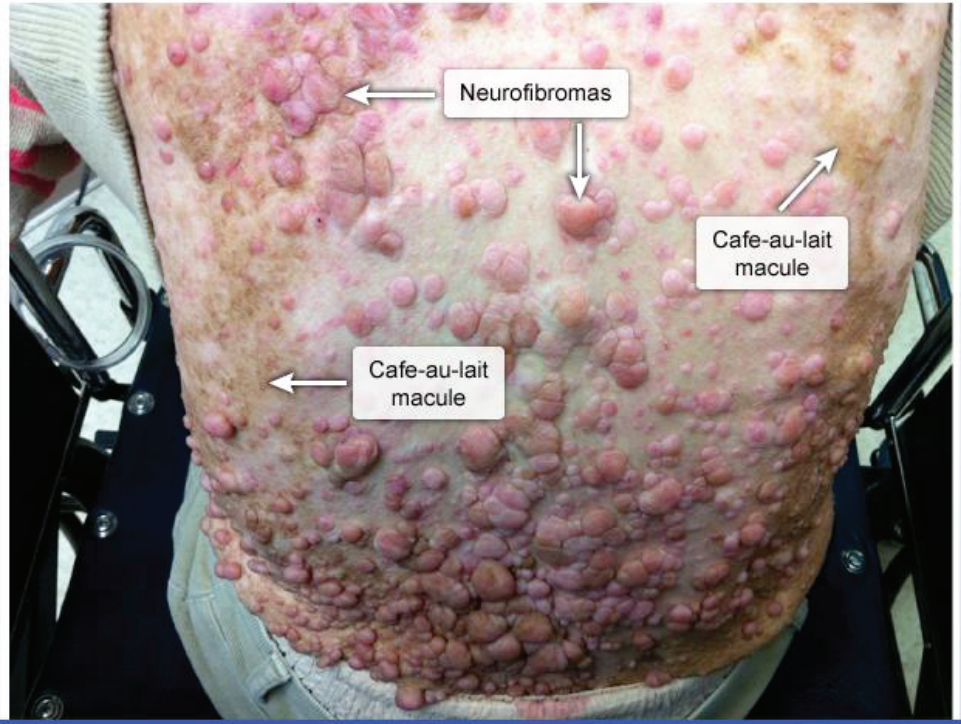
## Neurofibromatosis type 1



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The numerous fleshy, dome-shaped or pedunculated lesions shown in the image are cutaneous neurofibromas, a hallmark of neurofibromatosis type 1 (NF-1). This autosomal dominant condition is caused by a mutation in the NF1 gene, located on chromosome 17.

NF-1 has high penetrance (most patients who inherit the gene develop the disease), but the presentation is highly variable. All or none of the following symptoms may be present in an individual who suffers from NF-1:

1. Skin: **Café-au-lait spots** are hyperpigmented lesions with either smooth or irregular borders. The presence of axillary or inguinal freckles is another cutaneous feature of NF-1.
2. **Neurofibromas:** Short, sessile, or pedunculated lesions that vary in size. They are commonly multiple and distributed throughout the body.
3. Eye: Optic nerve gliomas may occur and cause visual loss. **Lisch nodules** are pigmented, asymptomatic hamartomas of the iris.
4. Bony abnormalities: These include sphenoid dysplasia, congenital **pseudoarthrosis**, and scoliosis.
5. Other associated tumors: Meningiomas, astrocytomas, gliomas, and pheochromocytomas. This patient's headaches and left leg weakness are probably the result of a brain tumor.


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presence of axillary or inguinal freckles is another cutaneous feature of NF-1.

2. **Neurofibromas:** Short, sessile, or pedunculated lesions that vary in size. They are commonly multiple and distributed throughout the body.
3. Eye: Optic nerve gliomas may occur and cause visual loss. **Lisch nodules** are pigmented, asymptomatic hamartomas of the iris.
4. Bony abnormalities: These include sphenoid dysplasia, congenital **pseudoarthrosis**, and scoliosis.
5. Other associated tumors: Meningiomas, astrocytomas, gliomas, and pheochromocytomas. This patient's headaches and left leg weakness are probably the result of a brain tumor.

**Educational objective:**

Neurofibromatosis type 1 is a single-gene autosomal-dominant disorder. It occurs due to mutation of the NF1 gene located on chromosome 17. Café-au-lait spots, multiple neurofibromas, and Lisch nodules are the most common symptoms.

| Genetics | Nervous System | Neurofibromatosis |
|---|---|---|
| Subject | System | Topic |

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A 65-year-old man comes to the emergency department with right upper and lower extremity weakness and slurred speech. The patient went to bed in his usual state of health and woke up with these symptoms. His medical problems include type 2 diabetes mellitus, hypertension, and hyperlipidemia. He takes atorvastatin, metformin, lisinopril, and low-dose aspirin. The patient has smoked a pack of cigarettes daily for the past 40 years. His temperature is 36.7 C (98 F), blood pressure is 160/90 mm Hg, and pulse is 118/min. He is mildly dysarthric with a right lower facial droop and right-sided hemiparesis. A noncontrast head CT is normal. Brain MRI reveals an acute subcortical infarct in the left internal capsule. Six months later, which of the following findings is most likely to be observed in the affected pyramidal tracts of this patient?

A. Calcification
B. Cytotoxic edema
C. Eosinophilic neurons
D. Hemorrhagic transformation
E. Neutrophilic infiltration



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A. Calcification
B. Cytotoxic edema
C. Eosinophilic neurons
D. Hemorrhagic transformation
E. Neutrophilic infiltration
F. Persistent myelin debris
G. Vasogenic edema

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- A. Calcification (33%)
- B. Cytotoxic edema (4%)
- C. Eosinophilic neurons (10%)
- D. Hemorrhagic transformation (7%)
- E. Neutrophilic infiltration (1%)
- F. Persistent myelin debris (34%)
- G. Vasogenic edema (7%)



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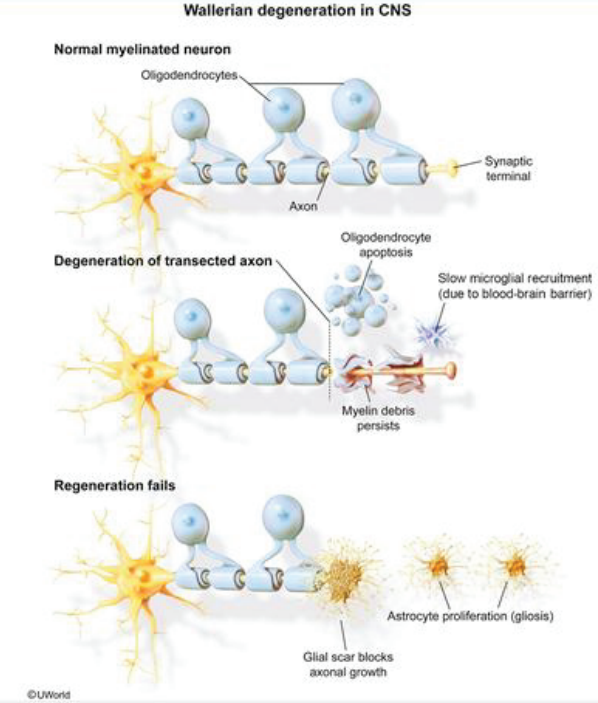


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**Wallerian degeneration** refers to the process that occurs when an axon is damaged, resulting in axonal degeneration and breakdown of the myelin sheath **distal to the site of injury**. Degeneration of the axon usually begins within a few days after lesion onset.

In the peripheral nervous system, Schwann cells sense the axonal degeneration and begin to degrade their myelin and secrete cytokines and chemokines that recruit macrophages. This allows effective clearance of myelin debris which, along with trophic factor secretion by Schwann cells, stimulates formation of a growth cone from the stump of the proximal axon and facilitates nerve regeneration.

In the **central nervous system**, phagocytic macrophages/microglia are recruited more slowly because of the blood-brain barrier. Myelin-producing oligodendrocytes also become inactive or undergo apoptosis and do not assist with phagocytosis. This slows removal of the **myelin debris**, which can **persist for years** in the degenerating tracts and **suppress axonal growth** via myelin-associated inhibitory factors. Astrocytes also release inhibitory molecules and proliferate in the weeks to months following injury, forming a **glial scar** that acts as a **barrier** to axon regeneration.

**(Choice A)** Calcification of an ischemic infarction may occur months to years after the event; however, this is a rare occurrence. Brain calcification is most commonly seen with certain neoplasms (eg, oligodendroglioma), infections (eg, neurocysticercosis), and vascular malformations.



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**scar** that acts as a **barrier** to axon regeneration.

**(Choice A)** Calcification of an ischemic infarction may occur months to years after the event; however, this is a rare occurrence. Brain calcification is most commonly seen with certain neoplasms (eg, oligodendroglioma), infections (eg, neurocysticercosis), and vascular malformations.

**(Choices B and G)** Cytotoxic and vasogenic edema typically occur in the acute setting after ischemic neuronal injury. Cytotoxic edema is a type of intracellular edema caused by impaired function of ATP-dependent sodium/potassium pumps on neuronal cell membranes. In contrast, vasogenic edema is a type of extracellular edema caused by increased vascular permeability due to the effects of pro-inflammatory cytokines.

**(Choice C)** In the first 12-24 hours after ischemic stroke, affected neurons classically shrink and develop intense cytoplasmic eosinophilia (red neurons) with pyknosis of the nucleus.

**(Choice D)** Embolic ischemic strokes have a high risk of undergoing acute hemorrhagic transformation within the first 7 days following the ischemic event.

**(Choice E)** Neutrophilic infiltration progressively increases up to 48 hours after ischemic stroke and then diminishes.


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**(Choice D)** Embolic ischemic strokes have a high risk of undergoing acute hemorrhagic transformation within the first 7 days following the ischemic event.

**(Choice E)** Neutrophilic infiltration progressively increases up to 48 hours after ischemic stroke and then diminishes.

**Educational objective:**

Wallerian degeneration refers to the process of axonal degeneration and breakdown of the myelin sheath that occurs distal to a site of injury. Axonal regeneration does not occur in the central nervous system due to the persistence of myelin debris, secretion of neuronal inhibitory factors, and development of dense glial scarring.

**References**

- Histopathological changes in acute ischemic stroke.
- Wallerian degeneration: gaining perspective on inflammatory events after peripheral nerve injury



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A 34-year-old man comes to the clinic with a 3-week history of difficulty hearing. He finds it increasingly difficult to tolerate everyday sounds. He also complains of ear pain and often avoids public places as a result. The patient has no past medical history and takes no medications. Injury to which of the following cranial nerves is most likely responsible for his condition?

A. Accessory
B. Facial
C. Glossopharyngeal
D. Hypoglossal
E. Vagus

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A 34-year-old man comes to the clinic with a 3-week history of difficulty hearing. He finds it increasingly difficult to tolerate everyday sounds. He also complains of ear pain and often avoids public places as a result. The patient has no past medical history and takes no medications. Injury to which of the following cranial nerves is most likely responsible for his condition?

A. Accessory (1%)
B. Facial (83%)
C. Glossopharyngeal (7%)
D. Hypoglossal (1%)
E. Vagus (6%)

Correct

83%
Answered correctly

29 secs
Time Spent

03/05/2021
Last Updated

Explanation



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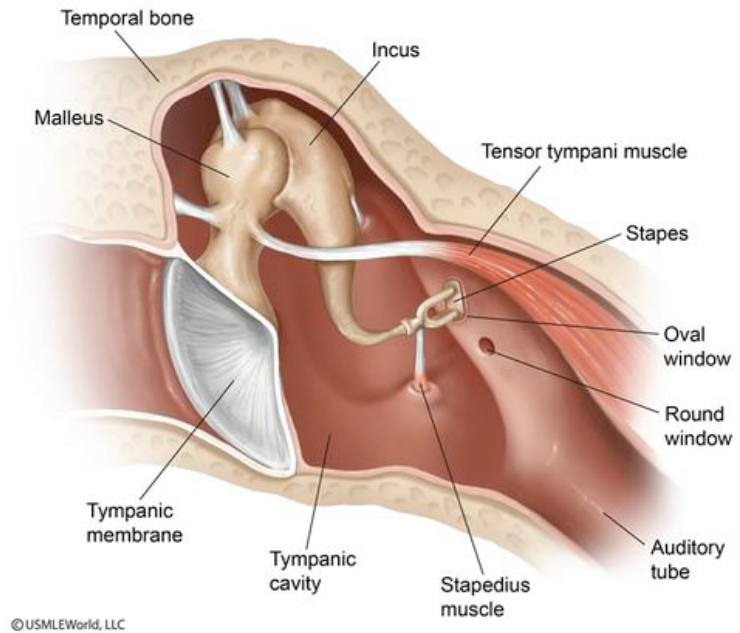
Middle ear anatomy

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The **middle ear cavity** contains 3 auditory ossicles (malleus, incus, and stapes) and 2 skeletal muscles (tensor tympani and stapedius) that participate in the transmission of sound from the tympanic membrane to the cochlea. The stapedius muscle arises from the wall of the tympanic cavity and inserts on the neck of the stapes. It is innervated by the **stapedius nerve**, a branch of the **facial nerve (CN VII)**. The stapedius muscle functions to stabilize the stapes; paralysis of the muscle (secondary to an injury or lesion to the facial nerve) causes the stapes to oscillate more widely, producing **hyperacusis**. Patients will typically complain of increased sensitivity to everyday sounds (eg, shutting doors, ringing phones, traffic) and will often withdraw socially as a result. Treatment consists of retraining (or sound) therapy using broadband noise (eg, "white noise").

The tensor tympani muscle arises from the cartilaginous portion of the auditory tube and the adjoining part of the sphenoid bone and inserts into the malleus. It functions to contract the tympanic membrane medially, thereby increasing its tension and dampening sound transmission. It is innervated by the mandibular branch of the trigeminal nerve (CN $V_3$).

Ipsilateral hyperacusis is a common finding associated with Bell's palsy (unilateral/peripheral facial paralysis).

**(Choices A, C, D, and E)** The accessory (CN XI), glossopharyngeal (CN IX), hypoglossal (CN XII), and


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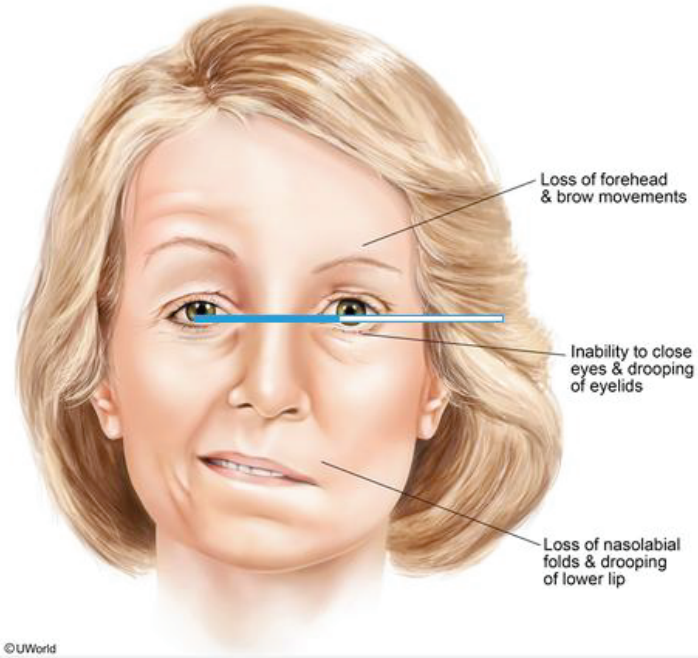
Peripheral facial palsy

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The tensor tympani muscle arises from the cartilaginous portion of the auditory tube and the adjoining part of the sphenoid bone and inserts into the malleus. It functions to contract the tympanic membrane medially, thereby increasing its tension and dampening sound transmission. It is innervated by the mandibular branch of the trigeminal nerve (CN $V_3$).

Ipsilateral hyperacusis is a common finding associated with Bell's palsy (unilateral/peripheral facial paralysis).

**(Choices A, C, D, and E)** The accessory (CN XI), glossopharyngeal (CN IX), hypoglossal (CN XII), and vagus (CN X) nerves are not associated with hyperacusis.

**Educational objective:**
The stapedius muscle is innervated by the stapedius nerve (a branch of the facial nerve). Paralysis of the stapedius muscle results in hyperacusis (eg, increased sensitivity to sound).

| Anatomy | Nervous System | Facial nerve |
|---|---|---|
| Subject | System | Topic |

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A 53-year-old man comes to the emergency department due to severe lower back pain. The patient's back pain started 2 weeks ago without any preceding trauma and has been keeping him awake at night. The pain has acutely worsened over the past 2 days and is not relieved with over-the-counter pain medications. His vital signs are within normal limits. Examination shows low back pain that is worse with back flexion and raising of the legs; it radiates into his left leg. Pinprick in the perianal area does not cause rapid contraction of the anal sphincter. The rest of the neurologic examination is normal. Which of the following nerve roots is most likely to be involved in this patient's condition?

- A. T12
- B. L2
- C. L4
- D. L5
- E. S1
- F. S4



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- A. T12 (0%)
- B. L2 (3%)
- C. L4 (5%)
- D. L5 (5%)
- E. S1 (25%)
- ✓ F. S4 (59%)

Correct

59%

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03/01/2021



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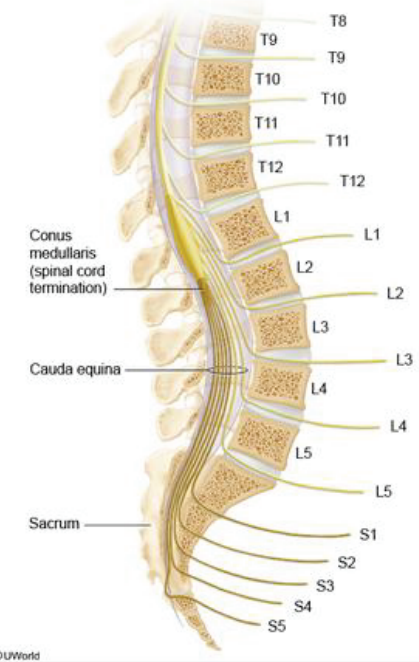
Relation of spinal nerve roots to vertebrae

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This patient's worsening low back pain with a positive straight leg test is consistent with subacute **lumbosacral radiculopathy**, which most often occurs due to a herniated disk; less common causes include neoplasm, fracture, or epidural hematoma/abscess. Compression of the spinal cord and/or nerve roots can cause a wide range of deficits based on the level(s) involved. This patient's **perianal anesthesia** with loss of the anocutaneous reflex indicates involvement of the **S2-S4** nerve roots.

In an adult, the spinal cord terminates in a tapering fashion as the **conus medullaris** (T12-S4) at the L1-L2 vertebral level. The collection of spinal nerves below this point (eg, L3-S4) exit inferiorly through their respective intervertebral foramina and are referred to as the **cauda equina** (ie, horse's tail). Lesions at the L1-L5 vertebral levels can affect the conus medullaris and/or T12-S4 nerve roots, resulting in a characteristic constellation of symptoms:

- **Radicular low back pain** (ie, radiates down one or both legs)
- Saddle/**perianal anesthesia** (S2-S4)
- Bowel and bladder dysfunction
- Lower extremity **weakness**

This pattern of neurologic deficits can occur with either conus medullaris syndrome (lesions around L1-L2


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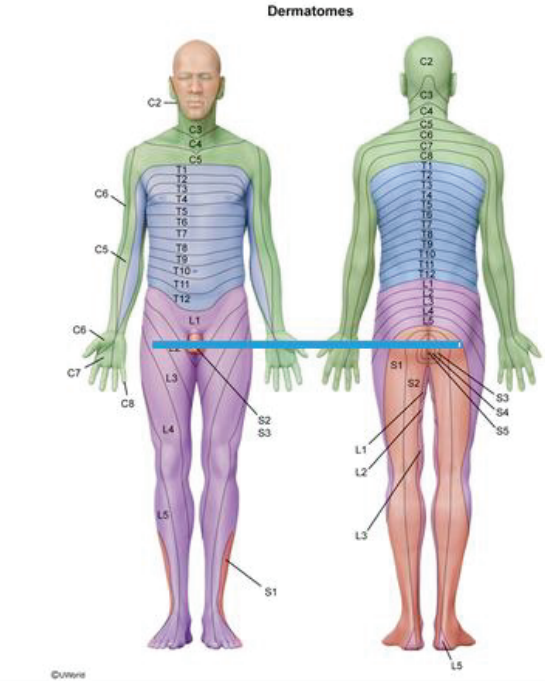


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This pattern of neurologic deficits can occur with either conus medullaris syndrome (lesions around L1-L2



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- Bowel and bladder dysfunction
- Lower extremity **weakness**

This pattern of neurologic deficits can occur with either conus medullaris syndrome (lesions around L1-L2 vertebrae) or cauda equina syndrome (lesions below L2 vertebra). **Conus medullaris syndrome** typically causes **bilateral**, symmetric lower extremity weakness with upper motor signs (eg, spasticity, hyperreflexia), while **cauda equina syndrome** tends to cause flaccid, **asymmetrical** lower extremity weakness. Due to the potential for further neurologic deterioration, affected patients require **urgent evaluation** including MRI of the spine.

**(Choice A)** Compression of the T12 nerve roots would result in lower abdominal or groin pain.

**(Choices B and C)** The L2-L4 spinal nerve roots contribute to the femoral nerve and mediate the quadriceps (ie, patellar) reflex. Lesions affecting these levels would cause loss of this reflex as well as anterior thigh sensory loss or paresthesia.

**(Choice D)** Lesions affecting the L5 nerve root would cause sensory loss or paresthesia over the lateral thigh and anterior calf.

**(Choice E)** The S1 nerve root supplies the Achilles reflex along with sensation to the posterior leg and posterolateral calf. Although the Achilles reflex can be affected in patients with lumbosacral radiculopathy,


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quadriceps (ie, patellar) reflex. Lesions affecting these levels would cause loss of this reflex as well as anterior thigh sensory loss or paresthesia.

**(Choice D)** Lesions affecting the L5 nerve root would cause sensory loss or paresthesia over the lateral thigh and anterior calf.

**(Choice E)** The S1 nerve root supplies the Achilles reflex along with sensation to the posterior leg and posterolateral calf. Although the Achilles reflex can be affected in patients with lumbosacral radiculopathy, this patient does not have evidence of S1 nerve root involvement on examination.

**Educational objective:**
Compressive lesions (eg, disk herniation, tumors) affecting the L1-L5 vertebral levels can impinge upon the conus medullaris and/or T12-S4 nerve roots, causing radicular low back pain, changes in bowel/bladder function, saddle/perianal anesthesia (eg, loss of anocutaneous reflex), and lower extremity weakness. Perianal sensation is carried by the S2-S4 nerve roots.

**References**

- Cauda equina syndrome.
- Definitions of traumatic conus medullaris and cauda equina syndrome: a systematic literature review



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A 6-year-old boy is brought to the office due to frequent nighttime awakenings. Several times a week over the past month, he has come to his parents' bed around 3 AM, frequently crying, appearing frightened, and saying that he became lost in a crowd and couldn't find his parents. Although he is comforted by their reassurance, he refuses to return to his room and eventually falls back asleep in their bed. The boy is about to start first grade at a new school. He is healthy and developmental milestones are normal. Examination shows no abnormalities. The sleep stage associated with this child's frightening experience is characterized by which of the following?

A. Increased duration in first third of the night
B. Low-amplitude theta EEG waves
C. Muscle paralysis
D. Sleep spindles and K complexes on EEG
E. Slow-wave sleep (delta EEG waves)

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A 6-year-old boy is brought to the office due to frequent nighttime awakenings. Several times a week over the past month, he has come to his parents' bed around 3 AM, frequently crying, appearing frightened, and saying that he became lost in a crowd and couldn't find his parents. Although he is comforted by their reassurance, he refuses to return to his room and eventually falls back asleep in their bed. The boy is about to start first grade at a new school. He is healthy and developmental milestones are normal. Examination shows no abnormalities. The sleep stage associated with this child's frightening experience is characterized by which of the following?

A. ~~Increased duration in first third of the night~~ (5%)

B. ~~Low-amplitude theta EEG waves~~ (5%)

C. Muscle paralysis (46%)

D. ~~Sleep spindles and K complexes on EEG~~ (17%)

E. Slow-wave sleep (delta EEG waves) (25%)

46%  01 min, 08 secs  02/05/2021



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This boy's recurrent awakenings with associated dream content and ability to be comforted are characteristic of **nightmares**, a common and developmentally normal experience for most children. Nightmares occur during **rapid eye movement (REM) sleep** and are more frequent in the **final third of the night** when REM periods become longer **(Choice A)**. Children can often describe the nightmare, become fully alert after awakening, and are typically able to be consoled. In contrast, sleep terrors are a common non-REM parasomnia of childhood that occur during slow-wave sleep in the first third of the night. Unlike nightmares, the child with sleep terrors does not fully awaken, is unresponsive to comfort, and has no associated dream content.

REM sleep is characterized by the defining feature of **rapid eye movements**, **vivid dreaming**, and **voluntary muscle atonia** due to inhibition of motor neurons. EEG activity during REM sleep is similar to the waking state, consisting of a combination of alpha, beta, and desynchronous EEG waves (sawtooth waves).

**(Choices B, D, and E)** These EEG findings are characteristic of different sub stages of non-REM sleep (typically divided into 3 stages). Theta waves are seen in stage 1 (transition from wakefulness to sleep) and stage 2 (light, stable sleep). Sleep spindles and K complexes are characteristic of stage 2. Delta waves are characteristic of slow-wave sleep or deep sleep (stage 3). Non-REM arousal disorders (eg


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(typically divided into 3 stages). Theta waves are seen in stage 1 (transition from wakefulness to sleep) and stage 2 (light, stable sleep). Sleep spindles and K complexes are characteristic of stage 2. Delta waves are characteristic of slow-wave sleep or deep sleep (stage 3). Non-REM arousal disorders (eg, sleep terrors) often occur in stage 3.

**Educational objective:**

REM sleep is characterized by dreaming and voluntary muscle paralysis, and occurs more often during the final third of the night. Nightmares occur during REM sleep and can be differentiated from sleep terrors, a non-REM parasomnia characterized by incomplete arousals and lack of recall of dream content.

**References**


- REM sleep at its core – circuits, neurotransmitters, and pathophysiology.
- Just a scary dream? A brief review of sleep terrors, nightmares, and rapid eye movement sleep behavior disorder.


| Pathophysiology | Nervous System | Parasomnias |
|---|---|---|
| Subject | System | Topic |

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A 45-year-old woman is evaluated for numbness and painful tingling of the right hand. The symptoms began 2 months ago and are especially prominent after she plays tennis. On examination, there is diminished sensation in the lateral palm, thenar eminence, and palmar aspect of the first 3½ digits of the right hand. This patient most likely has an injury involving a nerve that courses between which of the following structures?

A. Biceps and coracobrachialis muscles
B. Flexor carpi ulnaris and flexor digitorum profundus muscles
C. Humeral and ulnar heads of the pronator teres muscle
D. Olecranon and the medial epicondyle of the humerus
E. Supinator muscle and the head of the radius

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A 10-year-old boy is brought to the emergency department due to a fall while riding his bicycle. The patient hit his forehead on a concrete road barrier and sustained a laceration but did not lose consciousness. He reports no headache, nausea, vomiting, vision disturbances, or focal weakness or numbness. The patient received a tetanus vaccine at age 6. Vital signs are within normal limits. Physical examination reveals a 2-cm laceration above the left eyebrow. There are no other injuries. Neurologic examination shows no abnormalities. Prior to laceration repair with suture, lidocaine is injected in the subcutaneous tissue around the laceration. The patient reports immediate relief of pain, and there is loss of sensation to touch in the area infiltrated with the medication. These effects are most likely due to which of the following changes within the affected neurons?

A. Blockade of potassium channels
B. Blockade of sodium channels
C. Decreased calcium current
D. Increased chloride conductance
E. Interruption of axonal transport



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reports no headache, nausea, vomiting, vision disturbances, or focal weakness or numbness. The patient received a tetanus vaccine at age 6. Vital signs are within normal limits. Physical examination reveals a 2-cm laceration above the left eyebrow. There are no other injuries. Neurologic examination shows no abnormalities. Prior to laceration repair with suture, lidocaine is injected in the subcutaneous tissue around the laceration. The patient reports immediate relief of pain, and there is loss of sensation to touch in the area infiltrated with the medication. These effects are most likely due to which of the following changes within the affected neurons?

A. ~~Blockade of potassium channels~~ (2%)
B. Blockade of sodium channels (91%)
C. Decreased calcium current (2%)
D. Increased chloride conductance (2%)
E. Interruption of axonal transport (1%)

Correct

91%

01 min, 02 secs

09/28/2020



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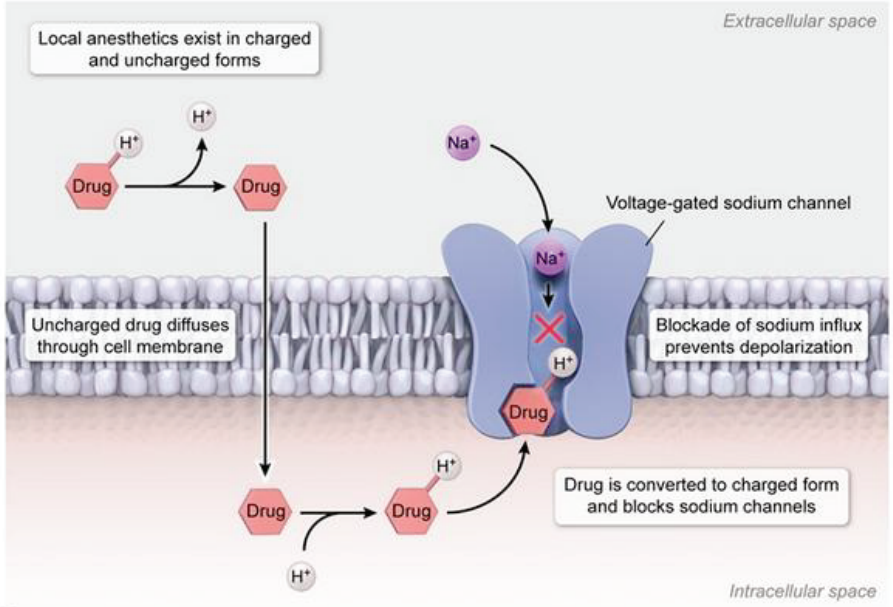
## Local anesthetic mechanism of action

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Lidocaine is a **local anesthetic** that interrupts nerve fiber transmission by **blocking sodium channels** in the neuronal cell membrane, preventing depolarization of the nerve. Local anesthetics have a greater effect on **small myelinated nerves**, so they preferentially inhibit neurons that carry pain and temperature sensation; pressure sensation and motor function are often preserved at typical doses.

Local anesthetics are **weak bases** that exist in charged and uncharged forms. When in the **uncharged form**, they diffuse through the cell membrane to block sodium channels from the inside of the cell. Increased acidity in the surrounding tissue, which occurs in infected wounds, results in more anesthetic molecules remaining in the charged form, rendering them unable to penetrate the cell membrane to exert an effect. Therefore, the dose required to achieve adequate anesthesia is higher in infected tissue.

**(Choice A)** Blockade of potassium channels would inhibit repolarization, thereby prolonging action potentials and increasing neurotransmitter release at the neuromuscular junction rather than halting action potential propagation.

**(Choice C)** Decreased calcium current slows the action potential propagation in cells that rely primarily on voltage-gated calcium channels for depolarization, such as cardiac slow response tissues (eg, sinoatrial and atrioventricular nodes); peripheral nerve depolarization is driven primarily by sodium, rather than



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**(Choice C)** Decreased calcium current slows the action potential propagation in cells that rely primarily on voltage-gated calcium channels for depolarization, such as cardiac slow response tissues (eg, sinoatrial and atrioventricular nodes); peripheral nerve depolarization is driven primarily by sodium, rather than calcium, influx.

**(Choice D)** GABA is the primary inhibitory neurotransmitter in the CNS. Activation of the GABA-A receptor, which is the target of some sedating medications (eg, benzodiazepines), activates voltage-gated chloride channels. The influx of chloride ions causes hyperpolarization, which inhibits action potentials.

**(Choice E)** Interruption of axonal transport delays the delivery of organelles (eg, mitochondria) and synaptic vesicles to the distal axon, causing impaired nerve impulse propagation. This occurs in some neurodegenerative diseases (eg, sporadic Alzheimer) or as an adverse effect of some chemotherapeutic agents (eg, vincristine).

**Educational objective:**
Local anesthetics diffuse through the neuronal cell membrane to block the influx of sodium into the cell. This prevents depolarization and inhibits action potential propagation.

**References**

- Molecular mechanisms of local anesthesia: a review.



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A 35-year-old female is hospitalized with headaches and vomiting. She has a long history of psychiatric illness and is known to practice eccentric dietary habits. Physical findings include papilledema, dry skin and hepatosplenomegaly. Head CT scan is ordered immediately but is negative for intracranial mass. Which of the following is a likely cause of this patient's condition?

A. Thiamine deficiency
B. Niacin deficiency
C. Vitamin $B_{12}$ deficiency
D. Riboflavin deficiency
E. Vitamin C overuse
F. Vitamin E overuse
G. Vitamin A overuse

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A 35-year-old female is hospitalized with headaches and vomiting. She has a long history of psychiatric illness and is known to practice eccentric dietary habits. Physical findings include papilledema, dry skin and hepatosplenomegaly. Head CT scan is ordered immediately but is negative for intracranial mass. Which of the following is a likely cause of this patient's condition?

- A. ~~Thiamine deficiency~~ (8%)
- B. ~~Niacin deficiency~~ (11%)
- C. ~~Vitamin $B_{12}$ deficiency~~ (5%)
- D. ~~Riboflavin deficiency~~ (4%)
- E. ~~Vitamin C overuse~~ (2%)
- F. Vitamin E overuse (5%)
- G. Vitamin A overuse (61%) ✓

Correct
61%
48 secs
01/30/2021


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Individuals who consume more than 10 times the Daily Value (Recommended Dietary Allowance) of vitamin A are prone to developing toxicity and may suffer hepatic injury so severe as to cause cirrhosis.

Vitamin A toxicity has been subdivided into three syndromes: acute, chronic, and teratogenic. The signs and symptoms of acute toxicity occur after the ingestion of a single high dose of vitamin A and include nausea, vomiting, vertigo, and blurred vision. The signs and symptoms of chronic toxicity occur after the long-term ingestion of high doses of vitamin A, and include alopecia, dry skin, hyperlipidemia, hepatotoxicity, hepatosplenomegaly, and visual difficulties. Papilledema, when present, is suggestive of cerebral edema in the setting of benign intracranial hypertension (pseudotumor cerebri). Teratogenic effects of excessive vitamin A ingestion include microcephaly, cardiac anomalies, and fetal death (especially in the first trimester of pregnancy).

**(Choice A)** Thiamine deficiency is associated with infantile and adult beriberi, as well as Wernicke-Korsakoff syndrome in alcoholics.

**(Choice B)** Niacin deficiency is characterized by the 3 D's of pellagra: (dementia, dermatitis, and diarrhea).

**(Choice C)** Vitamin $B_{12}$ (cobalamin) deficiency is frequently associated with pernicious anemia. The classic presentation of pernicious anemia is an older, mentally slow woman of northern European descent who is


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**(Choice C)** Vitamin $B_{12}$ (cobalamin) deficiency is frequently associated with pernicious anemia. The classic presentation of pernicious anemia is an older, mentally slow woman of northern European descent who is "lemon colored" (anemic and icteric), has a smooth, shiny tongue indicative of atrophic glossitis, and demonstrates a shuffling broad-based gait.

**(Choice D)** Vitamin B2 (riboflavin) deficiency is characterized by cheilosis, stomatitis, glossitis, dermatitis, corneal vascularization, and ariboflavinosis.

**(Choice E)** Large doses of vitamin C can give false negative stool guaiac results and are associated with diarrhea and abdominal bloating. Some studies suggest an association between high doses of vitamin C and calcium oxalate nephrolithiasis, though this remains controversial.

**(Choice F)** Large doses of vitamin E have been associated with higher mortality rates due to hemorrhagic stroke in adults and higher rates of necrotizing enterocolitis in infants.

**Educational Objective:**
Vitamin A overuse can result in intracranial hypertension, skin changes and hepatosplenomegaly.

| Biochemistry | Nervous System | Vitamin a toxicity |
|---|---|---|
| Subject | System | Topic |


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A 44-year-old man is brought to the emergency department by his wife because of confusion that began a few hours ago. Earlier in the day, he complained of a severe headache and nausea. On physical examination, his temperature is 38.3 C (101 F) and nuchal rigidity is present. Lumbar puncture and cerebrospinal fluid (CSF) examination show:

| | |
|---|---|
| Opening pressure | 300 mm $H_2O$ |
| Glucose | 20 mg/dL |
| Protein | 200 mg/dL |
| RBCs | 4 cells/μL |
| Leukocytes | 760 cells/μL |
| Neutrophils | 90% |
| Lymphocytes | 10% |

Gram stain of the CSF would most likely reveal which of the following?

A. Bean-shaped, Gram-negative cocci in pairs



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| Protein | 200 mg/dL |
| RBCs | 4 cells/μL |
| Leukocytes | 760 cells/μL |
| Neutrophils | 90% |
| Lymphocytes | 10% |

Gram stain of the CSF would most likely reveal which of the following?

A. Bean-shaped, Gram-negative cocci in pairs
B. Lancet-shaped, Gram-positive cocci in pairs
C. Gram-positive cocci in clusters
D. Non-motile Gram-negative coccobacilli
E. Motile Gram-positive rods

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|---|---|
| RBCs | 4 cells/μL |
| Leukocytes | 760 cells/μL |
| Neutrophils | 90% |
| Lymphocytes | 10% |

Gram stain of the CSF would most likely reveal which of the following?

A. Bean-shaped, Gram-negative cocci in pairs (29%)
B. Lancet-shaped, Gram-positive cocci in pairs (57%)
C. Gram-positive cocci in clusters (5%)
D. Non-motile Gram-negative coccobacilli (5%)
E. Motile Gram-positive rods (1%)

Correct

57%

01 min, 09 secs

02/12/2021



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A patient presenting with confusion, headache, fever, and nuchal rigidity should immediately raise suspicion for meningitis. In bacterial meningitis, cerebrospinal fluid (CSF) analysis typically shows elevated opening pressure, increased neutrophils, decreased glucose, and elevated protein. The morphology of any observed bacteria on CSF Gram stain provides an excellent preliminary identification of the pathogen (whereas cultures take time to grow).

***Streptococcus pneumoniae* is the most common cause of bacterial meningitis in adults of all ages** (see reference). On CSF Gram stain, lancet-shaped Gram-positive cocci are found in pairs. *S pneumoniae* meningitis often follows a pulmonary infection or mild upper respiratory infection. Alcoholics, sickle cell anemia patients, asplenic individuals, and those in generally poor health are at greater risk for *S pneumoniae* meningitis.

**(Choice A)** Bean-shaped Gram-negative cocci in pairs indicate *Neisseria meningitidis*. *N meningitidis* is the second most common cause of meningitis in patients < 60 years of age. *N meningitidis* tends to occur in outbreaks where many individuals live in close quarters (eg, army barracks and college dormitories).

**(Choice C)** Gram-positive cocci in clusters indicate *Staphylococcus* species. *Staphylococcus* is an unusual cause of community-acquired meningitis but is common in neurosurgical patients. It is thought that bacteria gain access to the meninges by direct inoculation during the procedure or postoperatively through


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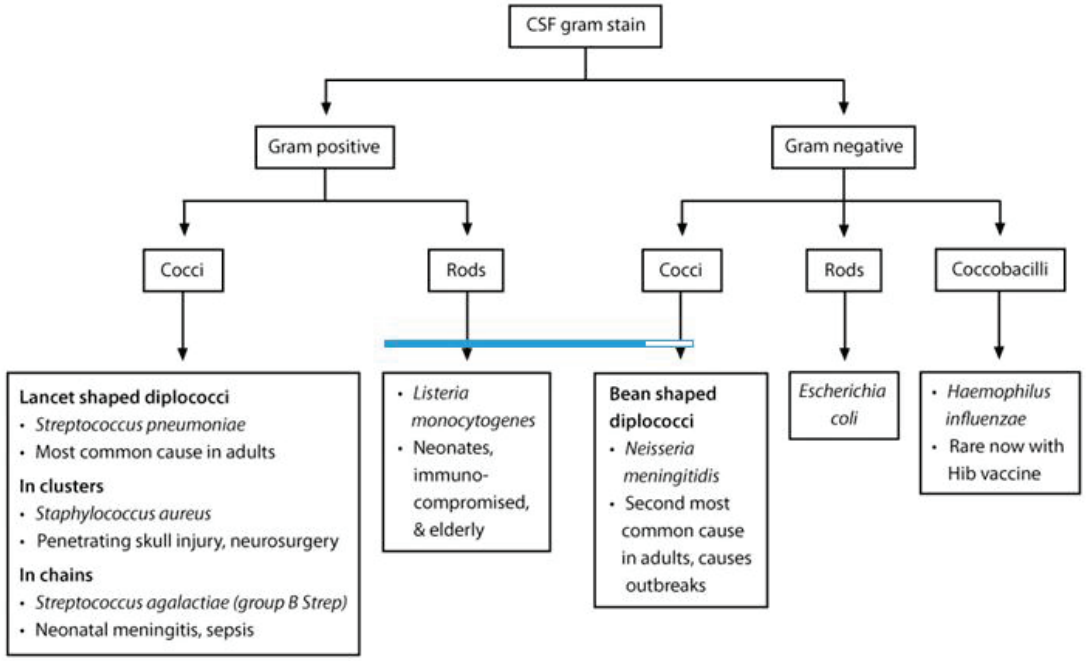


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**(Choice C)** Gram-positive cocci in clusters indicate *Staphylococcus* species. *Staphylococcus* is an unusual cause of community-acquired meningitis but is common in neurosurgical patients. It is thought that bacteria gain access to the meninges by direct inoculation during the procedure or postoperatively through the wound.

**(Choice D)** *Haemophilus influenzae* is a Gram-negative coccobacillus. *H influenzae* infection is becoming less common now that vaccination with the Hib capsule vaccine, a protein-capsule polysaccharide conjugate vaccine, has become widespread.

**(Choice E)** *Listeria monocytogenes* is a facultatively intracellular, motile, Gram-positive rod. It is the third most common cause of meningitis in neonates, after group B *Streptococci* and *Escherichia coli*. *Listeria* also causes meningitis in immunosuppressed patients and the elderly.

**Educational objective:**

Bacterial meningitis causes an increase in cerebrospinal fluid (CSF) neutrophil count and protein concentration as well as a decrease in CSF glucose. *Streptococcus pneumoniae* is a leading cause of community-acquired pneumonia, otitis media, and meningitis in adults. *S pneumoniae* appears on Gram stain as lancet-shaped, Gram-positive cocci in pairs.

**References**



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A 68-year-old woman is brought to the emergency department due to confusion and lower extremity weakness. The symptoms began 2 days ago along with fever, headache, malaise, and myalgias. Today, the patient was noted to be confused and had difficulty ambulating due to left lower extremity weakness. The patient has a history of lymphoma in remission, hypertension, and type 2 diabetes mellitus. She drinks alcohol socially but does not use tobacco or illicit drugs. She is visiting her family in Texas for the summer and has never traveled outside the United States. Temperature is 38.3 C (101 F), blood pressure is 130/70 mm Hg, and pulse is 96/min. The patient is oriented to place and person only and has a coarse hand tremor. There is flaccid paralysis of the left lower extremity with preserved sensation. CT scan of the head shows no abnormalities. Lumbar puncture is performed, and cerebrospinal fluid analysis shows lymphocytic pleocytosis and elevated protein. Cerebrospinal fluid polymerase chain reaction testing yields viral RNA. The agent infecting this patient most likely uses which of the following modes of transmission?

A. Blood transfusion
B. Fecal-oral
C. Insect bite
D. Respiratory



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The patient has a history of lymphoma in remission, hypertension, and type 2 diabetes mellitus. She drinks alcohol socially but does not use tobacco or illicit drugs. She is visiting her family in Texas for the summer and has never traveled outside the United States. Temperature is 38.3 C (101 F), blood pressure is 130/70 mm Hg, and pulse is 96/min. The patient is oriented to place and person only and has a coarse hand tremor. There is flaccid paralysis of the left lower extremity with preserved sensation. CT scan of the head shows no abnormalities. Lumbar puncture is performed, and cerebrospinal fluid analysis shows lymphocytic pleocytosis and elevated protein. Cerebrospinal fluid polymerase chain reaction testing yields viral RNA. The agent infecting this patient most likely uses which of the following modes of transmission?

A. Blood transfusion
B. Fecal-oral
C. Insect bite
D. Respiratory
E. Sexual

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The patient has a history of lymphoma in remission, hypertension, and type 2 diabetes mellitus. She drinks alcohol socially but does not use tobacco or illicit drugs. She is visiting her family in Texas for the summer and has never traveled outside the United States. Temperature is 38.3 C (101 F), blood pressure is 130/70 mm Hg, and pulse is 96/min. The patient is oriented to place and person only and has a coarse hand tremor. There is flaccid paralysis of the left lower extremity with preserved sensation. CT scan of the head shows no abnormalities. Lumbar puncture is performed, and cerebrospinal fluid analysis shows lymphocytic pleocytosis and elevated protein. Cerebrospinal fluid polymerase chain reaction testing yields viral RNA. The agent infecting this patient most likely uses which of the following modes of transmission?

A. ~~Blood transfusion~~ (2%)
B. Fecal-oral (34%)
C. Insect bite (35%)
D. Respiratory (21%)
E. ~~Sexual~~ (5%)

35%
02 mins, 10 secs
10/23/2020


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| West Nile virus | |
|---|---|
| **Clinical syndrome** | • West Nile fever: fever, headache, rash (maculopapular/morbilliform)<br>• Neuroinvasive: meningitis, encephalitis, acute asymmetric flaccid paralysis<br>  ◦ Parkinsonian symptoms (eg, rigidity, bradykinesia, tremor) |
| **Transmission** | • Mosquitoes (*Culex* spp.)<br>• More common in summer/fall<br>• Warm climate (southern United States, Latin America, Africa) |
| **Risk factors** | • Older age<br>• Malignancy/organ transplant |

This patient has acute confusion associated with fever and asymmetric lower extremity paralysis, consistent with neuroinvasive **West Nile virus** (WNV) infection. WNV is a positive-sense, single-strand RNA flavivirus transmitted by female **mosquitoes** (*Culex spp*), most commonly in the summer in warmer regions (eg, southern United States, Latin America, Africa). Most WNV infections are asymptomatic or present with a flu-like illness (ie, West Nile fever: fever, headache, myalgias), often with a maculopapular or


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morbilliform rash on the back and chest.

**Neuroinvasive** infection is an uncommon complication of WNV but has a 10% fatality rate. It occurs most commonly in older patients and those with a history of malignancy or organ transplant, and is characterized by meningitis (ie, headache, meningismus) and/or encephalitis (altered mental status). The presence of acute-onset **asymmetric flaccid paralysis** is highly suggestive of WNV, particularly if the patient demonstrates concurrent **parkinsonian features** (eg, rigidity, bradykinesia, tremor, postural instability). Diagnosis can be made when compatible clinical findings are associated with positive cerebrospinal fluid **anti-WNV antibodies** (polymerase chain reaction testing often not needed).

**(Choices A and E)** HIV, cytomegalovirus, and Epstein-Barr virus can be transmitted via blood transfusion or sexual contact, whereas herpes simplex virus 1 and 2 are transmitted through sexual or oral contact. Although these viruses can cause aseptic meningitis and encephalitis, asymmetric flaccid paralysis and concurrent tremor are more suggestive of WNV.

**(Choice B)** The enteroviruses, so named due to their fecal-oral transmission, account for most aseptic meningitis cases, but most are very rarely associated with flaccid paralysis. Of the enteroviruses, poliovirus can cause paralysis but would be extremely unlikely (eradicated in the United States). Post-polio syndrome can occur in patients with prior infection, but it generally causes slowly progressive weakness


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meningitis cases, but most are very rarely associated with flaccid paralysis. Of the enteroviruses, poliovirus can cause paralysis but would be extremely unlikely (eradicated in the United States). Post-polio syndrome can occur in patients with prior infection, but it generally causes slowly progressive weakness without acute fever, confusion, or rash.

**(Choice D)** Varicella, mumps, and adenoviruses are spread via respiratory secretions and are capable of causing aseptic meningitis or encephalitis, but paralysis is rare.

**Educational objective:**

West Nile virus is a single-strand flavivirus transmitted by mosquitoes, most commonly in the summer. Most infections are asymptomatic or may present with a flu-like illness (West Nile fever), often with a maculopapular or morbilliform rash. Neuroinvasive disease manifests as meningitis, encephalitis, or asymmetric flaccid paralysis; patients may have parkinsonian features.

**References**

- West Nile virus: review of the literature.

| Microbiology | Nervous System | West Nile virus infection |
|---|---|---|
| Subject | System | Topic |

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A 35-year-old, right-handed mechanic comes to the clinic due to progressive right hand weakness. The patient frequently uses a screwdriver at work. Neurologic examination shows preserved sensation in the upper limbs. There is weakness on extension of the fingers and thumb in the right hand. Strength is otherwise intact. Triceps reflexes are 2+ and bilaterally symmetric. The nerve affected in this patient was most likely injured at which of the following locations?

A. Axilla
B. Carpal tunnel
C. Coracobrachialis
D. Hook of hamate
E. Midshaft of the humerus
F. Supinator muscle

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A 35-year-old, right-handed mechanic comes to the clinic due to progressive right hand weakness. The patient frequently uses a screwdriver at work. Neurologic examination shows preserved sensation in the upper limbs. There is weakness on extension of the fingers and thumb in the right hand. Strength is otherwise intact. Triceps reflexes are 2+ and bilaterally symmetric. The nerve affected in this patient was most likely injured at which of the following locations?

A. ~~Axilla~~ (1%)
B. ~~Carpal tunnel~~ (20%)
C. Coracobrachialis (5%)
D. ~~Hook of hamate~~ (11%)
E. ~~Midshaft of the humerus~~ (17%)
✓ F. Supinator muscle (43%)

Correct

43%
Answered correctly

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Time Spent

02/15/2021
Last Updated



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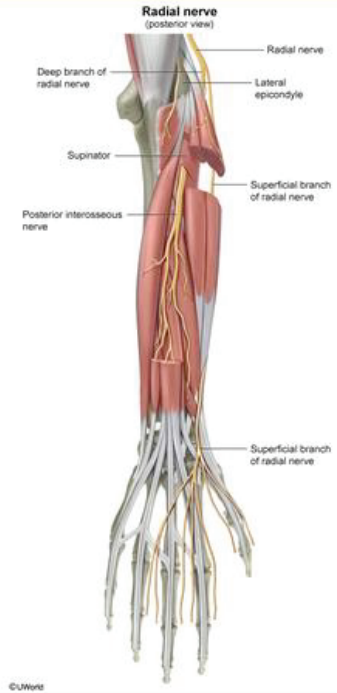
## Exhibit Display

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The radial nerve enters the forearm anterior to the lateral epicondyle and divides into superficial and deep branches. The superficial branch provides purely somatic sensory innervation to the radial half of the dorsal hand, and the deep branch innervates the extensor compartment muscles in the forearm. After passing between the superficial and deep parts of the **supinator muscle**, the deep branch continues as the posterior interosseous nerve, which innervates muscles involved in finger and thumb extension.

Injury to the deep branch of the radial nerve at the supinator muscle may occur due to **repetitive pronation/supination** of the forearm (eg, frequent screwdriver use), direct trauma, or dislocation of the head of the radius. Patients typically have **weakness on finger and thumb extension** (ie, finger drop). The triceps brachii (responsible for elbow extension and triceps reflex) and extensor carpi radialis longus (responsible for wrist extension) are typically unaffected because the branches supplying these muscles diverge proximal to the supinator muscle. Cutaneous **sensory branches** are similarly **preserved**.

**(Choices A and E)** Injury to the radial nerve at the axilla (eg, crutch palsy) typically causes weakness of the forearm, hand, and finger extensor muscles (eg, wrist drop) with absent triceps reflex and sensory loss over the posterior arm, forearm, and dorsolateral hand. Injury to the nerve at the midshaft humerus (eg, radial groove) usually causes similar forearm/hand deficits with sparing of the triceps muscle.

**(Choice B)** Carpal tunnel syndrome can result from any condition that reduces the size of the carpal



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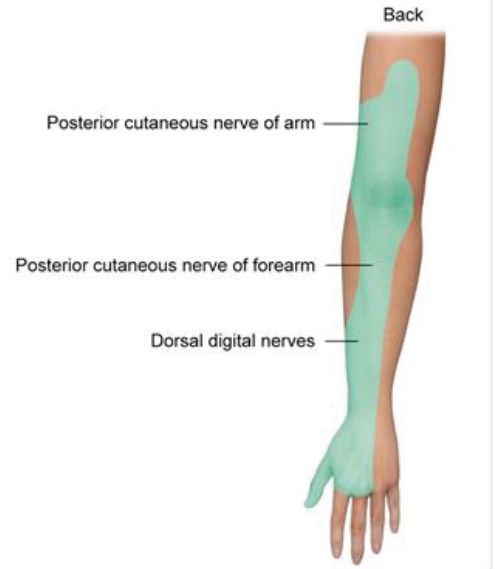
## Exhibit Display

### Radial nerve

| Motor function | Cutaneous innervation |
|---|---|
| • Extension at elbow, wrist and fingers<br>• Forearm supination<br>• Thumb abduction in plane of palm |  |



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(Choice B) Carpal tunnel syndrome can result from any condition that reduces the size of the carpal



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**(Choice B)** Carpal tunnel syndrome can result from any condition that reduces the size of the carpal tunnel and compresses the median nerve (eg, pregnancy, hypothyroidism). Patients typically have pain/paresthesia affecting the first 3 and a half digits along with thenar atrophy and thumb abduction/opposition weakness as the disease progresses.

**(Choice C)** The coracobrachialis muscle lies deep to the biceps brachii and is innervated by the musculocutaneous nerve. Nerve injury may result in decreased strength on forearm flexion and sensory loss over the lateral forearm.

**(Choice D)** In the wrist, the ulnar nerve passes between the hook of hamate and the pisiform bone in the Guyon canal. Ulnar nerve injury at this site can cause weakness on finger abduction/adduction and clawing of the fourth and fifth digits.

**Educational objective:**

Injury to the radial nerve at the supinator muscle may occur due to repetitive pronation/supination of the forearm, direct trauma, or subluxation of the radius. Patients typically have weakness during finger and thumb extension (ie, finger-drop) without wrist drop or sensory deficits.

**References**

- Clinical features of wrist drop caused by compressive radial neuropathy and its anatomical



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A 23-year-old man comes to the physician at his girlfriend's insistence. She says that the patient's frequent snoring keeps her up at night and that in the last 4 months he has twice fallen asleep while they were talking. In this same period, the patient says that he has regularly fallen asleep in the afternoon while reading or watching television but typically feels refreshed after a brief nap. When asked whether he experiences any other symptoms, the patient hesitantly reveals that he sometimes hears a voice call his name prior to falling asleep. He also reports uncharacteristic episodes of clumsiness in which he has suddenly dropped objects or fallen to his knees. Examination shows no abnormalities. Which of the following is the most likely diagnosis in this patient?

A. Brief psychotic disorder
B. Delayed sleep-wake phase disorder
C. Idiopathic hypersomnia
D. Insufficient sleep
E. Narcolepsy
F. Obstructive sleep apnea



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A. Brief psychotic disorder
B. Delayed sleep-wake phase disorder
C. Idiopathic hypersomnia
D. Insufficient sleep
E. Narcolepsy
F. Obstructive sleep apnea
G. REM sleep behavior disorder



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reading or watching television but typically feels refreshed after a brief nap. When asked whether he experiences any other symptoms, the patient hesitantly reveals that he sometimes hears a voice call his name prior to falling asleep. He also reports uncharacteristic episodes of clumsiness in which he has suddenly dropped objects or fallen to his knees. Examination shows no abnormalities. Which of the following is the most likely diagnosis in this patient?

A. ~~Brief psychotic disorder~~ (0%)
B. ~~Delayed sleep-wake phase disorder~~ (1%)
C. ~~Idiopathic hypersomnia~~ (1%)
D. ~~Insufficient sleep~~ (1%)
✓ E. Narcolepsy (84%)
F. Obstructive sleep apnea (7%)
G. ~~REM sleep behavior disorder~~ (2%)

Correct
84%
01 min, 18 secs
02/13/2021


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| Narcolepsy | |
|---|---|
| **DSM-5 diagnostic criteria** | • Recurrent lapses into sleep or naps (≥3 times/week for 3 months)<br>• ≥1 of the following:<br>◦ Cataplexy: Brief loss of muscle tone precipitated by strong emotion (eg, laughter, excitement)<br>◦ Low cerebrospinal fluid levels of hypocretin-1<br>◦ Shortened REM sleep latency |
| **Associated features** | • Hypnagogic or hypnopompic hallucinations<br>• Sleep paralysis |

**Narcolepsy** is a chronic sleep disorder characterized by frequent, overwhelming urges to sleep. It is commonly associated with **cataplexy**, a sudden loss of muscle tone that occurs in response to intense (usually positive) emotions. Narcolepsy results from the depletion of hypocretin (also known as orexin)-secreting neurons in the lateral hypothalamus that are involved in maintaining wakefulness.

Patients with narcolepsy experience shortened sleep latency and typically enter rapid eye movement (REM) sleep almost immediately. They commonly experience intrusions of REM sleep phenomena during


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(REM) sleep almost immediately. They commonly experience intrusions of REM sleep phenomena during sleep-wake transitions, including **hypnagogic** (upon falling asleep) and **hypnopompic** (upon awakening) **hallucinations** and **sleep paralysis** (inability to move immediately after awakening). The clinical diagnosis of narcolepsy can be confirmed by **low cerebrospinal fluid** levels of **hypocretin-1** or shortened REM sleep latency on polysomnography.

**(Choice A)** This patient is experiencing hypnagogic hallucinations, which are characteristic of narcolepsy. Brief psychotic disorder is diagnosed when one or more positive psychotic symptoms are present for less than a month in the absence of another medical disorder or substance use.

**(Choice B)** Delayed sleep-wake phase disorder most often presents in adolescence and is characterized by intact duration and quality of sleep that is shifted to a later bedtime and wake time.

**(Choice C)** Idiopathic hypersomnia is diagnosed when excessive and impairing daytime sleepiness cannot be explained by another sleep disorder. Patients with idiopathic hypersomnia have persistent daytime sleepiness rather than "sleep attacks." Unlike patients with narcolepsy, they typically do not feel refreshed after naps.

**(Choice D)** Insufficient sleep may result in excessive daytime sleepiness, napping, and quicker REM onset, but it is not associated with cataplexy or sleep-related hallucinations.



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**(Choice D)** Insufficient sleep may result in excessive daytime sleepiness, napping, and quicker REM onset, but it is not associated with cataplexy or sleep-related hallucinations.

**(Choice F)** Obstructive sleep apnea, the most common cause of excessive daytime sleepiness, is characterized by loud snoring, gasping, and apneas during sleep. It is caused by upper airway obstruction and is not associated with cataplexy, sleep-related hallucinations, or sleep paralysis.

**(Choice G)** Patients with REM sleep behavior disorder lose normal sleep paralysis during REM sleep and, as a result, act out the content of their dreams (eg, punching, kicking).

**Educational objective:**
Narcolepsy is a chronic sleep disorder characterized by excessive daytime sleepiness, cataplexy, and REM sleep-related phenomena (ie, hypnagogic/hypnopompic hallucinations, sleep paralysis).

**References**


- Narcolepsy.
- Diagnosis and management of narcolepsy.




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A 21-year-old woman comes to the office due to a long history of episodic headaches, dizziness, and gait imbalance. The headaches are located in the occipital region, are characterized as dull, and last for several hours. Physical examination reveals gait ataxia but no focal weakness or sensory loss. MRI of the brain shows low-lying cerebellar tonsils extending below the plane of the foramen magnum into the vertebral canal. Which of the following is the most likely cause of this patient's condition?

A. Autoimmune disease
B. Congenital malformation
C. Germline mutation
D. Neoplastic disease
E. Sequelae of prior trauma
F. Vascular disease

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A. Autoimmune disease (1%)
B. Congenital malformation (87%)
C. Germline mutation (0%)
D. Neoplastic disease (5%)
E. Sequelae of prior trauma (3%)
F. Vascular disease (1%)

Correct

87% Answered correctly

44 secs Time Spent

12/25/2020 Last Updated



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**Chiari malformations** are a group of **congenital** disorders caused by underdevelopment of the posterior fossa. The small size of the fossa causes parts of the **cerebellum** and medulla to **herniate through** the **foramen magnum**. There are 2 types of Chiari malformations. Chiari type I is the most common and benign, and is characterized by low-lying cerebellar tonsils that extend below the foramen magnum into the vertebral canal. Patients typically present during adolescence/adulthood with paroxysmal occipital headaches (due to meningeal irritation) and cerebellar dysfunction (eg, dizziness, ataxia) due to compression of the cerebellar tonsils.

Chiari type II, Arnold-Chiari malformation, is more severe and typically becomes evident during the neonatal period. It is characterized by downward displacement of the cerebellum (vermis, tonsils) and medulla through the foramen magnum. Non-communicating hydrocephalus almost always occurs due to aqueductal stenosis. Compression of the medulla may result in dysphagia, stridor, and apnea. Patients also often have an associated lumbar myelomeningocele, which can cause lower limb paralysis.

**(Choice A)** Multiple sclerosis is an autoimmune demyelinating disorder of the central nervous system that typically presents in young adult women with neurologic deficits disseminated in space and time. Neuroimaging typically shows periventricular white matter lesions.

**(Choice C)** Friedreich ataxia is an autosomal recessive trinucleotide repeat disorder that presents during


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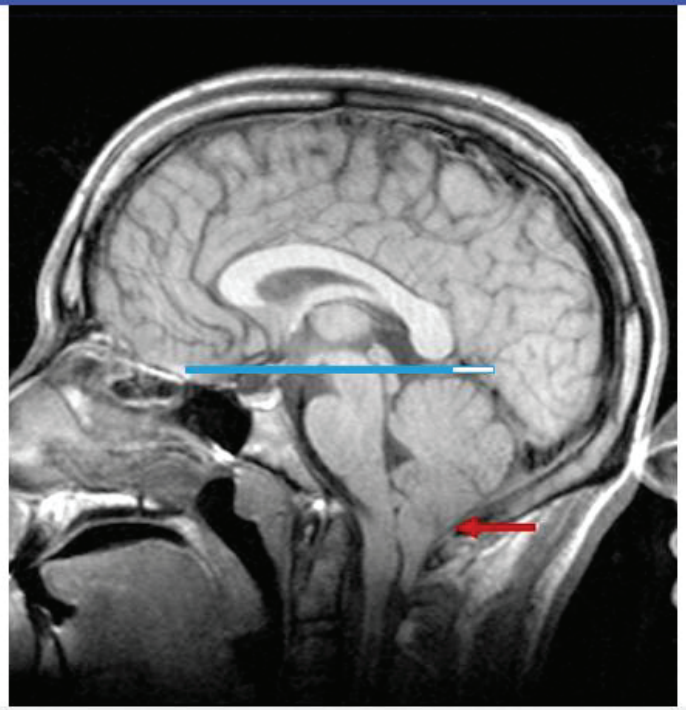

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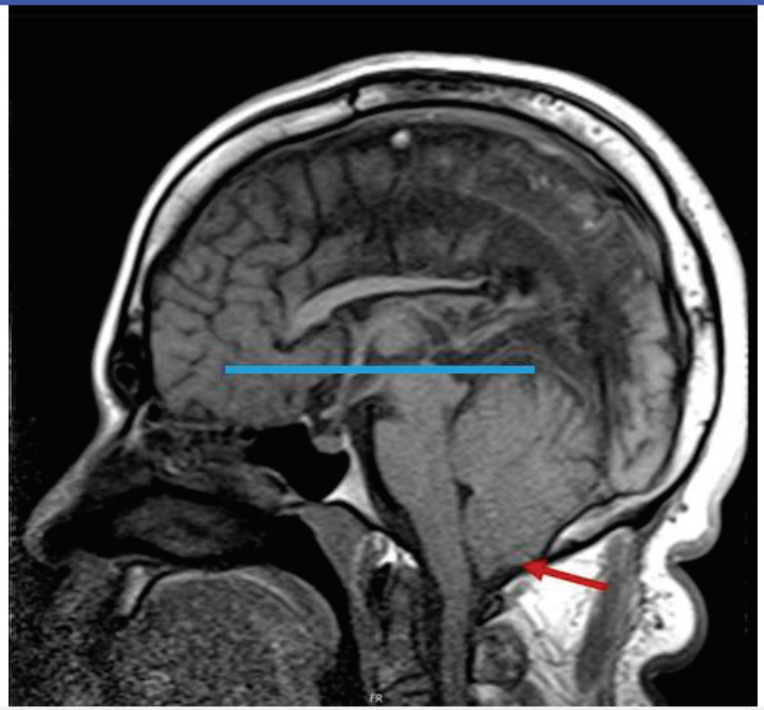

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**(Choice C)** Friedreich ataxia is an autosomal recessive trinucleotide repeat disorder that presents during childhood with ataxia, loss of vibration/proprioception sense, and skeletal abnormalities (eg, kyphoscoliosis, pes cavus).

**(Choice D)** Cerebellar neoplasms (eg, medulloblastoma, pilocytic astrocytoma) often present in children with symptoms of increased intracranial pressure (eg, headache, vomiting) and cerebellar dysfunction. However, the absence of a cerebellar tumor on neuroimaging makes this unlikely.

**(Choice E)** Traumatic brain injury can cause headache and neurologic impairment; however, this patient's MRI findings are highly characteristic of Chiari type I malformation.

**(Choice F)** Cerebellar stroke may present with acute-onset occipital headache, dizziness, and ataxia. However, this patient's young age, absence of cardiovascular risk factors, and long history of episodic symptoms make this less likely.

**Educational objective:**
Chiari malformations are congenital disorders that result from underdevelopment of the posterior fossa, causing parts of the cerebellum and medulla to herniate through the foramen magnum. Chiari type I is relatively benign and presents during adulthood with occipital headache and cerebellar dysfunction. Chiari type II is a more severe form that affects neonates and is often associated with lumbar myelomeningocele


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**Educational objective:**

Chiari malformations are congenital disorders that result from underdevelopment of the posterior fossa, causing parts of the cerebellum and medulla to herniate through the foramen magnum. Chiari type I is relatively benign and presents during adulthood with occipital headache and cerebellar dysfunction. Chiari type II is a more severe form that affects neonates and is often associated with lumbar myelomeningocele and hydrocephalus.

**References**



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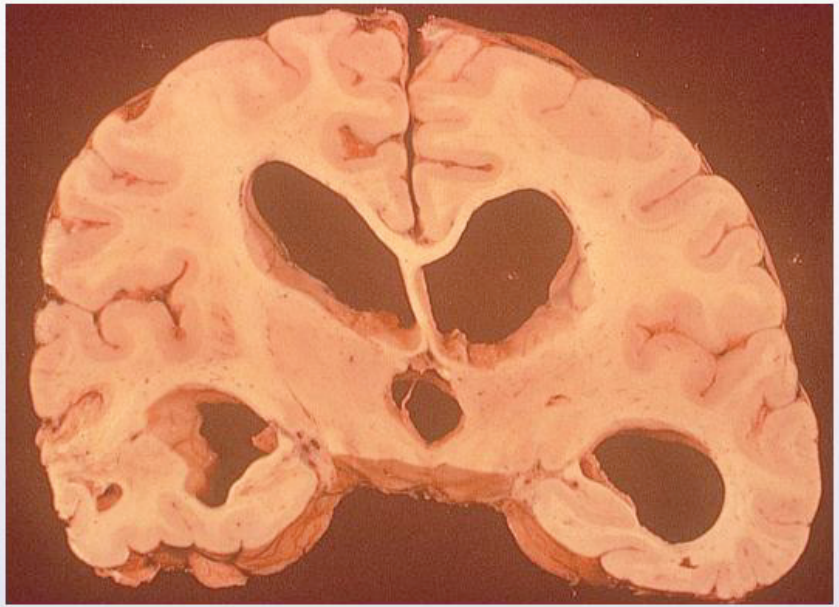
A gross brain section of a 54-year-old male who suffered from severe tuberculous meningitis is shown below.



This patient's condition is most likely related to impaired function of which of the following?



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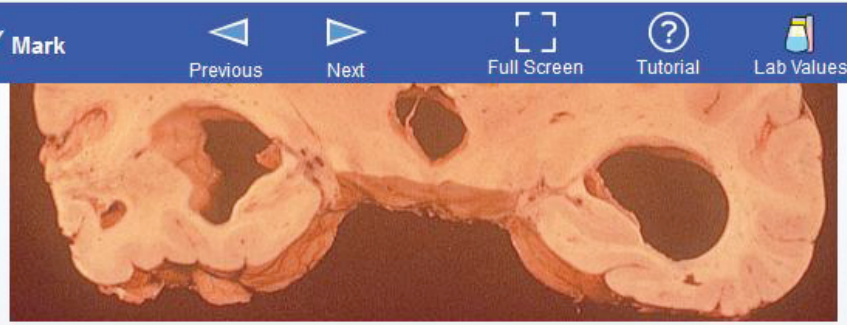

This patient's condition is most likely related to impaired function of which of the following?

A. Emissary veins
B. Arachnoid trabeculae
C. Arachnoid granulations
D. Choroid plexus
E. Dural septae
F. Communicating arteries

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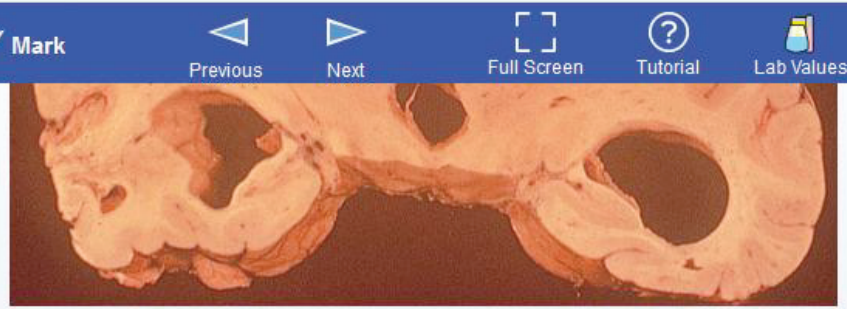

This patient's condition is most likely related to impaired function of which of the following?

A. ~~Emissary veins~~ (2%)

B. Arachnoid trabeculae (6%)

✓ C. Arachnoid granulations (67%)

✗ D. Choroid plexus (17%)

E. ~~Dural septae~~ (2%)

F. ~~Communicating arteries~~ (3%)

Incorrect
Correct answer

67%

01 min, 37 secs

12/22/2020



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Cerebrospinal fluid (CSF) is secreted by the choroid plexus of the lateral and fourth ventricles. The path of CSF flow is as follows: lateral ventricles → interventricular foramen of Monro → the third ventricle → cerebral aqueduct → the fourth ventricle → the foramina of Luschka and Magendie → subarachnoid space. In the subarachnoid space, CSF is absorbed by arachnoid granulations and then enters the venous sinuses. The dynamic balance between production and absorption of CSF allows stable intracranial volume (120-150 ml) and pressure (50-180 mm $H_2O$).

If the normal flow of CSF from the ventriculi to the subarachnoid space is disrupted, **non-communicating hydrocephalus** occurs. Ventriculi above the obstruction are enlarged, while those below the obstruction are normal. Congenital anomalies, such as aqueductal stenosis, Arnold-Chiari or Dandy-Walker malformations, cause non-communicating hydrocephalus. In all cases, the obstacle to CSF flow exists within the ventriculi.

In **communicating hydrocephalus**, there is no obstruction to CSF flow from the ventriculi to the subarachnoid space. Communicating hydrocephalus usually occurs secondary to dysfunction or obliteration of subarachnoid villi. This dysfunction is usually a sequelae of meningeal infections (including tuberculosis meningitis, as in this patient) or subarachnoid/intraventricular hemorrhage. In communicating hydrocephalus, all ventriculi are symmetrically enlarged, as in the image above.



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obliteration of subarachnoid villi. This dysfunction is usually a sequelae of meningeal infections (including tuberculosis meningitis, as in this patient) or subarachnoid/intraventricular hemorrhage. In communicating hydrocephalus, all ventriculi are symmetrically enlarged, as in the image above.

**(Choice A)** The emissary veins pass through apertures between the intracranial sinuses and veins outside the cranial vault. They do not participate in absorption of CSF.

**(Choice B)** Arachnoid trabeculae pass from the arachnoid through the subarachnoid space to the pia mater. They are not involved in the metabolism of CSF.

**(Choice D)** The choroid plexus is the site of CSF secretion; in communicating hydrocephalus, CSF absorption, not secretion, is impaired. If present, a choroid plexus papilloma might cause a symmetric ventricular enlargement that appears virtually identical to communicating hydrocephalus. Communicating hydrocephalus is far more common than choroid plexus papilloma, however, making Choice D a plausible answer, but not the most likely one.

**(Choices E and F)** Neither dural septae nor communicating arteries are implicated in the pathogenesis of communicating hydrocephalus.

**Educational Objective:**
Symmetrical enlargement of the ventriculi is characteristic of communicating hydrocephalus.


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mater. They are not involved in the metabolism of CSF.

**(Choice D)** The choroid plexus is the site of CSF secretion; in communicating hydrocephalus, CSF absorption, not secretion, is impaired. If present, a choroid plexus papilloma might cause a symmetric ventricular enlargement that appears virtually identical to communicating hydrocephalus. Communicating hydrocephalus is far more common than choroid plexus papilloma, however, making Choice D a plausible answer, but not the most likely one.

**(Choices E and F)** Neither dural septae nor communicating arteries are implicated in the pathogenesis of communicating hydrocephalus.

**Educational Objective:**
Symmetrical enlargement of the ventriculi is characteristic of communicating hydrocephalus.
Communicating hydrocephalus usually occurs secondary to dysfunction or obliteration of subarachnoid villi. This dysfunction is usually a sequelae of meningeal infection (including tuberculosis meningitis) or subarachnoid/intraventricular hemorrhage.

| Pathology | Nervous System | Hydrocephalus |
|---|---|---|
| Subject | System | Topic |



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A 38-year-old Caucasian female presents to your office because of sudden episodes of severe, right-sided facial pain. She describes the pain as "a knife stabbing my face." The pain lasts several seconds and is usually instigated by a meal or teeth brushing. There is no nausea or vomiting. She denies any visual changes. Her past medical history is significant for hyperlipidemia. She drinks alcohol socially and does not use tobacco. She has no family history of facial pain. Her vital signs are within normal limits, and physical examination shows no rash. Which of the following is the best initial treatment for this patient?

A. Baclofen
B. Haloperidol
C. Diazepam
D. Carbamazepine
E. Propranolol
F. Phenobarbital
G. Valproic acid



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A. Baclofen (13%)
B. Haloperidol (2%)
C. Diazepam (6%)
✓ D. Carbamazepine (64%)
E. Propranolol (4%)
F. Phenobarbital (3%)
G. Valproic acid (6%)

64%
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This case presents a classic picture of trigeminal neuralgia (tic douloureux). This condition presents with episodes of sudden and severe pain in the distribution of CN V (particularly V2 and V3). The pain is described as "stabbing" or like an "electrical shock"; it is usually unilateral, and does not last more than few seconds; but occurs repeatedly. Pain is triggered by any stimulus to CN V, for example chewing, teeth brushing, shaving or washing an affected area of the face, swallowing, or exposure to hot or cold temperatures. These painful episodes may occur for several months. In the majority of cases, trigeminal neuralgia is not caused by any structural abnormality and its pathogenesis remains unclear.

Carbamazepine is the drug of choice for the treatment of trigeminal neuralgia. It is effective in pain reduction in up to 80% of patients. Like phenytoin, it inhibits neuronal high-frequency firing by reducing the ability of sodium channels to recover from inactivation. Carbamazepine can cause aplastic anemia, so CBC should be monitored regularly. Carbamazepine is a P450 inducer that increases the metabolism of many other medications, thereby decreasing their effectiveness.

**(Choices A and G)** Baclofen and valproic acid can be used for trigeminal neuralgia, but are not first-line choices.

**(Choice B)** Haloperidol is a neuroleptic medication used for the treatment of schizophrenia, acute


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choices.

**(Choice B)** Haloperidol is a neuroleptic medication used for the treatment of schizophrenia, acute psychoses, acute mania, and Tourette syndrome. It is not indicated in trigeminal neuralgia.

**(Choice E)** Propranolol has various uses, including migraine prophylaxis and the reduction of portal venous pressure to prevent variceal bleed. It is not used for trigeminal neuralgia.

**(Choice F)** Phenobarbital is effective for the management of generalized tonic-clonic seizures. It is not used for trigeminal neuralgia.

**Educational objective:**
Trigeminal neuralgia presents with brief episodes of sudden and severe "electric shock-like" or "stabbing" pain in the distribution of CN V (particularly V2 and V3). Carbamazepine is the drug of choice.

**References**

- Trigeminal neuralgia and its management
- Drug therapy of trigeminal neuralgia

Pharmacology Nervous System Trigeminal neuralgia



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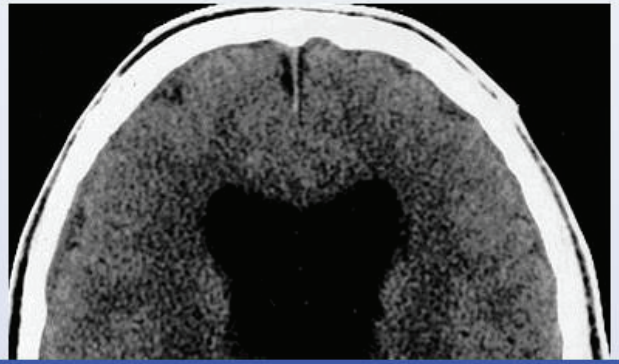
A 64-year-old woman is evaluated for progressive gait disturbance over the last 2 years. The patient feels her feet are "stuck on the floor" and that she is unsteady while walking. She also recently began experiencing urinary urgency and has wet herself several times due to difficulty getting to the bathroom on time. The patient stopped working 6 months ago because of difficulty concentrating, and she has also lost interest in her hobbies and social activities. She has had no tremor, visual changes, headaches, nausea, or vomiting. The patient has a remote history of closed traumatic brain injury. Vital signs are within normal limits. On physical examination, lower extremity tone and deep tendon reflexes are increased. Sensation to light touch, pain, and vibration are normal. The patient's gait is slow with small steps and a wide base. CT scan of the head is shown below.





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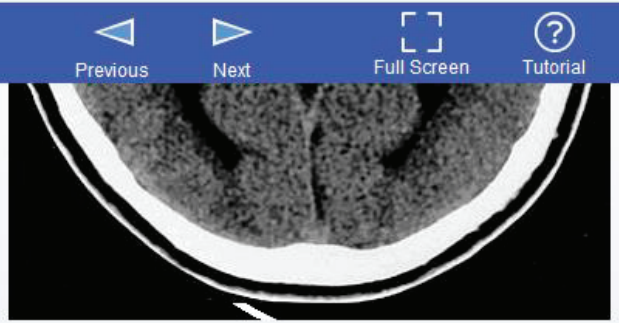

Which of the following is the most likely diagnosis?

A. Alzheimer disease

B. Frontotemporal dementia

C. Idiopathic Parkinson disease

D. Major depressive disorder

E. Normal pressure hydrocephalus

F. Obstructive hydrocephalus

G. Vitamin $B_{12}$ deficiency



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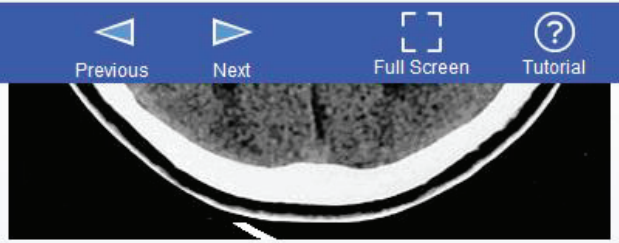

Which of the following is the most likely diagnosis?

- A. Alzheimer disease (1%)
- B. Frontotemporal dementia (0%)
- C. Idiopathic Parkinson disease (2%)
- D. Major depressive disorder (0%)
- ✓ E. Normal pressure hydrocephalus (85%)
- F. Obstructive hydrocephalus (10%)
- G. Vitamin $B_{12}$ deficiency (0%)

Correct

85%
Answered correctly

59 secs
Time Spent

09/27/2020
Last Updated



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This patient's CT scan demonstrates **ventriculomegaly** out of proportion to sulci enlargement, consistent with **normal pressure hydrocephalus** (NPH). NPH is a form of communicating hydrocephalus associated with decreased cerebrospinal fluid (CSF) resorption by the arachnoid granulations. It may be idiopathic or occur secondary to prior brain trauma (as in this patient), infection, or subarachnoid hemorrhage, resulting in scarring of the arachnoid granulations. As CSF accumulates, the ventricles progressively expand to accommodate the increasing volume, thereby maintaining normal intracranial pressure.

Symptoms of NPH are progressive and occur due to the disruption of periventricular white matter tracts by the expanding ventricles. Characteristic features include the following:

- **Gait difficulties** appear early in the disease course and are characterized by slow, short steps with decreased height. The feet may appear as though stuck to the ground (magnetic gait). Upper motor neuron signs (eg, spasticity, hyperreflexia) may also be evident.
- **Cognitive disturbances**, such as difficulty concentrating and apathy, usually become more apparent as the disease advances.
- **Urinary incontinence** is typically from urinary urgency. As the disease progresses, patients may develop apathy toward incontinence.


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Symptoms often improve in response to large-volume CSF removal, and long-term treatment frequently involves placement of a ventriculoperitoneal shunt.

**(Choice A)** Alzheimer disease typically presents with memory deficits out of proportion to other cognitive domains. Although ventricular enlargement may be seen on imaging as the disease progresses, it occurs in proportion to sulci enlargement and is the result of generalized brain atrophy (hydrocephalus ex-vacuo).

**(Choice B)** Frontotemporal dementia causes memory deficits but primarily causes personality changes and aphasia. Neuroimaging demonstrates atrophy of the frontal and temporal lobes.

**(Choice C)** Parkinson disease causes gait abnormalities but is also typically associated with resting tremor and cogwheel rigidity. Cognitive deficits occur later in the disease course.

**(Choice D)** Major depressive disorder can be associated with impaired concentration and loss of interest in activities (anhedonia). However, other features (eg, depressed mood, sleep disturbance) are not evident in this patient. In addition, neuroimaging and neurologic examination are typically normal.

**(Choice F)** Noncommunicating (obstructive) hydrocephalus is typically associated with congenital abnormalities (eg, aqueductal stenosis) and tumors. It causes ventriculomegaly but is associated with elevated intracranial pressure (eg, headache, nausea/vomiting).


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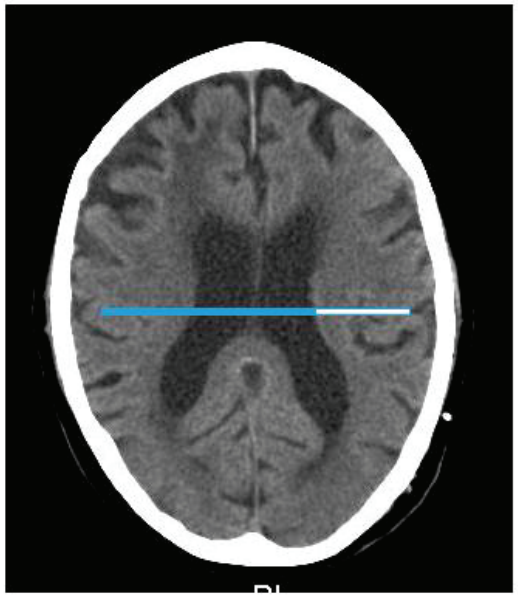

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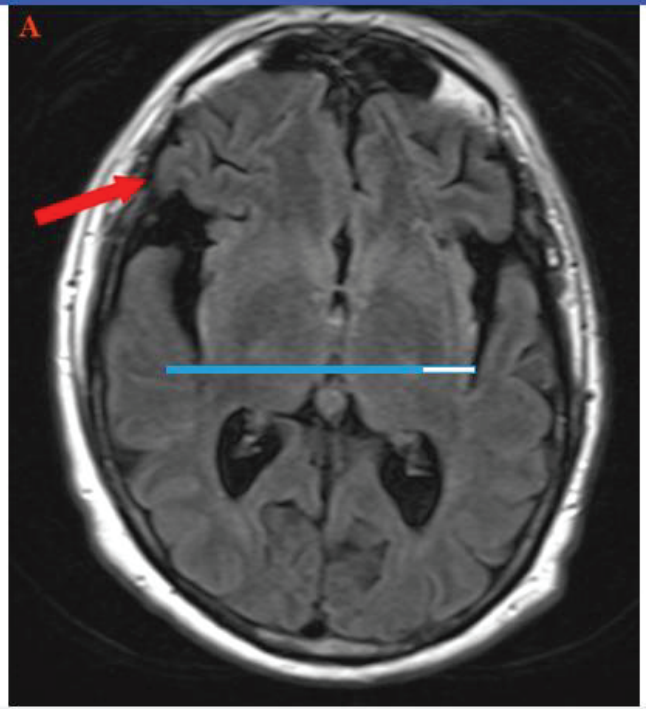


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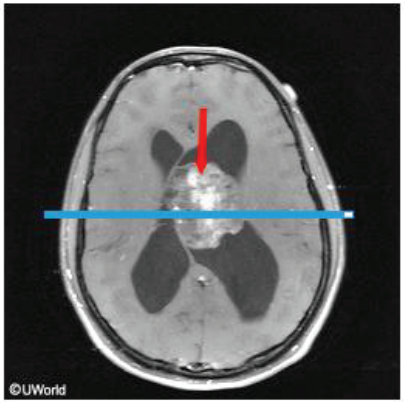


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in this patient. In addition, neuroimaging and neurologic examination are typically normal.

**(Choice F)** Noncommunicating (obstructive) hydrocephalus is typically associated with congenital abnormalities (eg, aqueductal stenosis) and tumors. It causes ventriculomegaly but is associated with elevated intracranial pressure (eg, headache, nausea/vomiting).

**(Choice G)** Vitamin $B_{12}$ deficiency can cause dementia but is typically associated with peripheral neuropathy (eg, abnormal position, vibration sense) and glossitis. Although MRI of the spinal cord can show degeneration of the posterior columns, CT scan of the head would be expected to be normal.

**Educational objective:**

Normal pressure hydrocephalus presents with progressive gait difficulties, cognitive disturbances, and urinary incontinence. It is a form of communicating hydrocephalus characterized by ventriculomegaly without persistent elevations in intercranial pressure. Brain imaging reveals ventricular enlargement out of proportion to sulci enlargement.

**References**

- A review of cognitive impairment and differential diagnosis in idiopathic normal pressure hydrocephalus.

Pathology Nervous System Normal pressure hydrocephalus



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A 55-year-old, right-handed woman is brought to the emergency department due to acute-onset headache and difficulty with vision. En route to the hospital, she becomes unconscious. Medical history is significant for hypertension. Blood pressure is 150/90 mm Hg and pulse is 90/min and regular. CT scan of the head without contrast demonstrates an acute hemorrhage in the left temporal lobe with compression of the anterior medial temporal lobe against the free margin of the tentorium cerebelli. Which of the following cranial nerves is most likely to be compromised in this patient?

A. Abducens
B. Facial
C. Oculomotor
D. Optic
E. Trigeminal
F. Trochlear
G. Vagus



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and difficulty with vision. En route to the hospital, she becomes unconscious. Medical history is significant for hypertension. Blood pressure is 150/90 mm Hg and pulse is 90/min and regular. CT scan of the head without contrast demonstrates an acute hemorrhage in the left temporal lobe with compression of the anterior medial temporal lobe against the free margin of the tentorium cerebelli. Which of the following cranial nerves is most likely to be compromised in this patient?

A. ~~Abducens~~ (7%)
B. Facial (6%)
C. Oculomotor (56%)
D. ~~Optic~~ (13%)
E. ~~Trigeminal~~ (6%)
F. ~~Trochlear~~ (6%)
G. ~~Vagus~~ (3%)

Correct
56%
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10/20/2020


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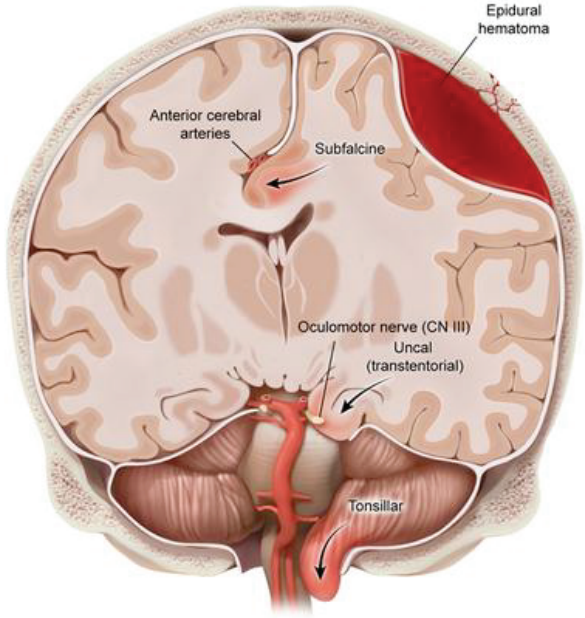
Types of brain herniation

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The cranial vault is formed by the cranial bones and divided into compartments by the dural folds (ie, falx cerebri, tentorium cerebelli). Because the cranial vault is rigid, there is minimal space for brain expansion if a **rapidly enlarging mass** (eg, hemorrhage, tumor) or severe, generalized edema (eg, traumatic brain injury) develops. As a result, portions of the **brain** may **protrude** through the **openings in the dural folds**, often according to the following **herniation** patterns:

- Subfalcine: herniation of the cingulate gyrus under the falx cerebri
- Uncal: herniation of the medial temporal lobe (ie, uncus) through the tentorial notch
- Tonsillar: herniation of the cerebellar tonsils through the foramen magnum

This patient with compression of the anterior medial temporal lobe against the free margin of the tentorium cerebelli has **uncal herniation**. As uncal herniation progresses, the following may occur:

- **Ipsilateral oculomotor nerve** (CN III) compression leads to an **ipsilateral fixed and dilated pupil**. Paralysis of the oculomotor muscles occurs later and leads to ptosis and a down-and-out position of the ipsilateral eye.
- Ipsilateral posterior cerebral artery compression leads to **contralateral homonymous hemianopsia**


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- Ipsilateral posterior cerebral artery compression leads to **contralateral homonymous hemianopsia** with macular sparing.
- Compression of the **ipsilateral cerebral peduncle** of the midbrain against the tentorium may occur, damaging descending corticospinal tracts and causing **contralateral hemiparesis**.
- As the midbrain is pushed toward the contralateral side, the contralateral cerebral peduncle may also become compressed against the tentorium, causing ipsilateral hemiparesis (false localizing sign).

Without prompt treatment, further pressure on the midbrain can cause downward brainstem displacement (eg, central herniation) and brainstem hemorrhages (ie, Duret hemorrhages) from stretching and rupture of paramedian branches of the basilar artery. This is usually fatal.

**(Choices A, B, D, E, F, and G)** None of the other cranial nerves become compressed due to uncal herniation.

**Educational objective:**
Uncal herniation is a possible complication of an expanding ipsilateral mass lesion (eg, hemorrhage, tumor). The first sign of uncal herniation is a fixed, dilated pupil on the side of the lesion. Contralateral or ipsilateral hemiparesis and contralateral homonymous hemianopsia with macular sparing may also occur.


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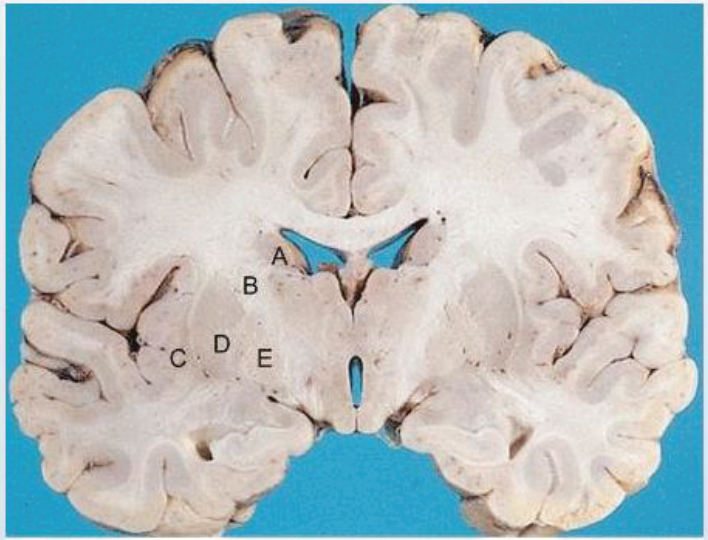
A 62-year-old man comes to the office with right arm clumsiness. Physical examination reveals motor weakness involving the right arm and leg. The patient's speech is slurred, and there is drooping of the right lower face. On passive flexion of the right arm, there is initial resistance followed by a sudden release of tension as flexion is continued. A lesion affecting which of the following brain structures is most likely responsible for this patient's condition?

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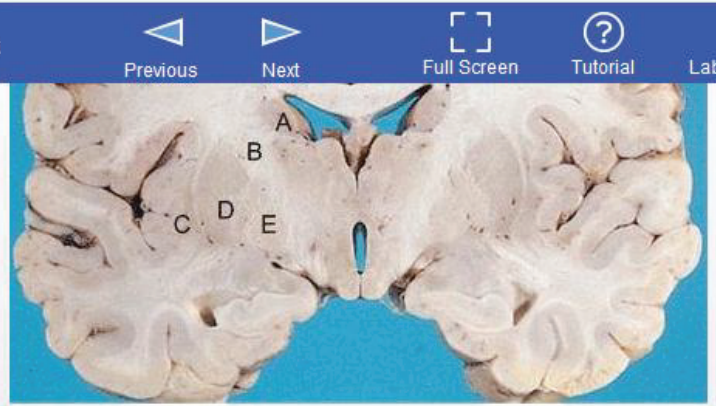


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- A.A
- B.B
- C.C
- D.D
- E.E

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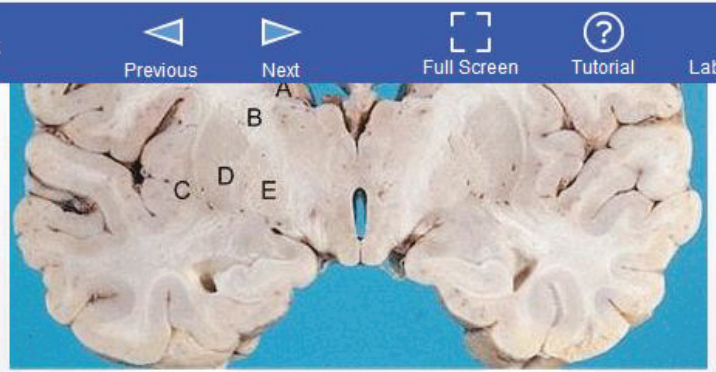


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- A.A (7%)
- ✓ B.B (60%)
- C.C (7%)
- D.D (12%)
- E.E (11%)

Correct

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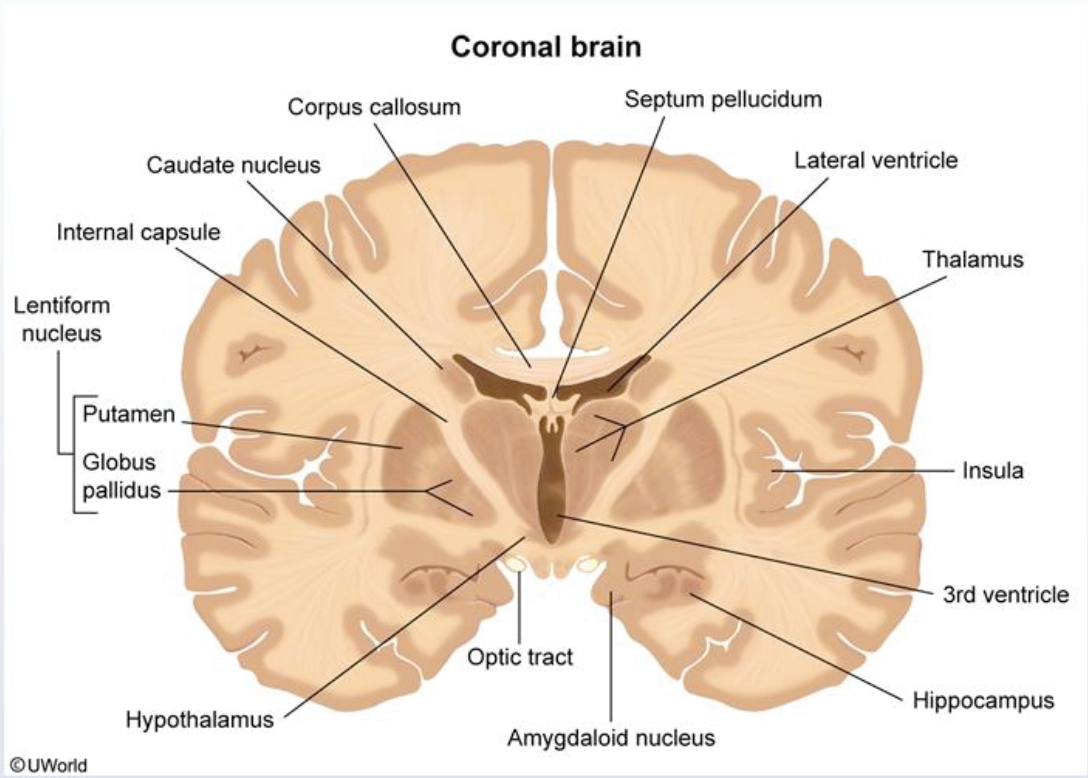


This patient has **clasp-knife spasticity**, which is characterized by initial resistance to passive flexion



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This patient has **clasp-knife spasticity**, which is characterized by initial resistance to passive flexion followed by a sudden release of resistance. This form of spasticity is seen with **upper motor neuron lesions** and results from a lack of upper motor neuron inhibition on the spinal stretch reflex arc. With passive arm flexion, the extensor muscles are activated by the **disinhibited stretch reflex**, causing initial resistance that can be overcome with continued flexion.

Upper motor neuron lesions can affect any part of the **pyramidal motor system** (eg, corticobulbar/corticospinal tracts), which runs from the precentral gyrus (primary motor cortex) through the internal capsule to the brainstem and spinal cord. Patients with an **internal capsule stroke** can have both sensory and motor deficits, but most commonly have pure **motor weakness** affecting the **contralateral arm**, **leg**, **and lower face** as well as clasp-knife spasticity, hyperreflexia, and a positive Babinski sign.

**(Choices A, D, and E)** The caudate nucleus, putamen, and globus pallidus (ie, basal ganglia) are part of the extrapyramidal motor system, which regulates both voluntary and involuntary motor function (eg, posture, muscle tone, prevention of erratic movements). Lesions to these structures can result in motor dysfunction, including chorea (ie, random, jerky, uncontrollable movements), tremor, bradykinesia, or rigidity, as well as changes in cognition and behavior.

**(Choice C)** The insular cortex (insula) plays a role in consciousness and emotion (along with the limbic



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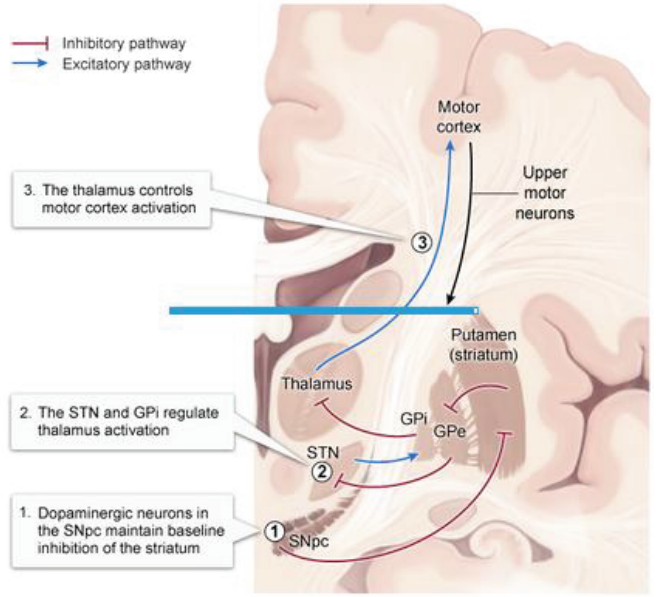
This patient has clasp-knife spasticity, which is characterized by initial resistance to passive flexion

Exhibit Display

Normal basal ganglia motor pathways




**GPe** = globus pallidus externus; **GPi** = globus pallidus internus;
**SNpc** = substantia nigra pars compacta; **STN** = subthalamic nucleus.

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**(Choices A, D, and E)** The caudate nucleus, putamen, and globus pallidus (ie, basal ganglia) are part of the extrapyramidal motor system, which regulates both voluntary and involuntary motor function (eg, posture, muscle tone, prevention of erratic movements). Lesions to these structures can result in motor dysfunction, including chorea (ie, random, jerky, uncontrollable movements), tremor, bradykinesia, or rigidity, as well as changes in cognition and behavior.

**(Choice C)** The insular cortex (insula) plays a role in consciousness and emotion (along with the limbic system), autonomic nervous system control, and awareness of visceral sensations.

**Educational objective:**

Upper motor neuron lesions (ie, internal capsule stroke) cause contralateral weakness with clasp-knife spastic rigidity, hyperreflexia, and a positive Babinski sign. These lesions damage the pyramidal motor system (eg, corticospinal tracts), which runs from the precentral gyrus (primary motor cortex) through the internal capsule to the brainstem and spinal cord.

**References**

- Pathology of lacunar ischemic stroke in humans--a systematic review.

Anatomy Nervous System Ischemic stroke



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An 18-year-old previously healthy woman is brought to the emergency department with 2 days of fever, headache, and lethargy. She has also had nausea and several episodes of vomiting. Her temperature is 38.9 C (102 F), blood pressure is 110/60 mm Hg, and pulse is 108/min. On physical examination, the patient is diaphoretic, delirious, and has a petechial rash on the trunk and extremities. Signs of meningeal irritation are present. CT scan of the head reveals no mass lesions. She is scheduled for a lumbar puncture for cerebrospinal fluid analysis. During this procedure, which of the following anatomical landmarks helps locate the optimal site for needle insertion?

A. Anterior superior iliac spine
B. Costal margin
C. Iliac crest
D. Inferior angle of the scapula
E. Posterior superior iliac spine

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An 18-year-old previously healthy woman is brought to the emergency department with 2 days of fever, headache, and lethargy. She has also had nausea and several episodes of vomiting. Her temperature is 38.9 C (102 F), blood pressure is 110/60 mm Hg, and pulse is 108/min. On physical examination, the patient is diaphoretic, delirious, and has a petechial rash on the trunk and extremities. Signs of meningeal irritation are present. CT scan of the head reveals no mass lesions. She is scheduled for a lumbar puncture for cerebrospinal fluid analysis. During this procedure, which of the following anatomical landmarks helps locate the optimal site for needle insertion?

A. Anterior superior iliac spine (13%)
B. Costal margin (2%)
✓ C. Iliac crest (61%)
D. Inferior angle of the scapula (0%)
E. Posterior superior iliac spine (21%)

61%
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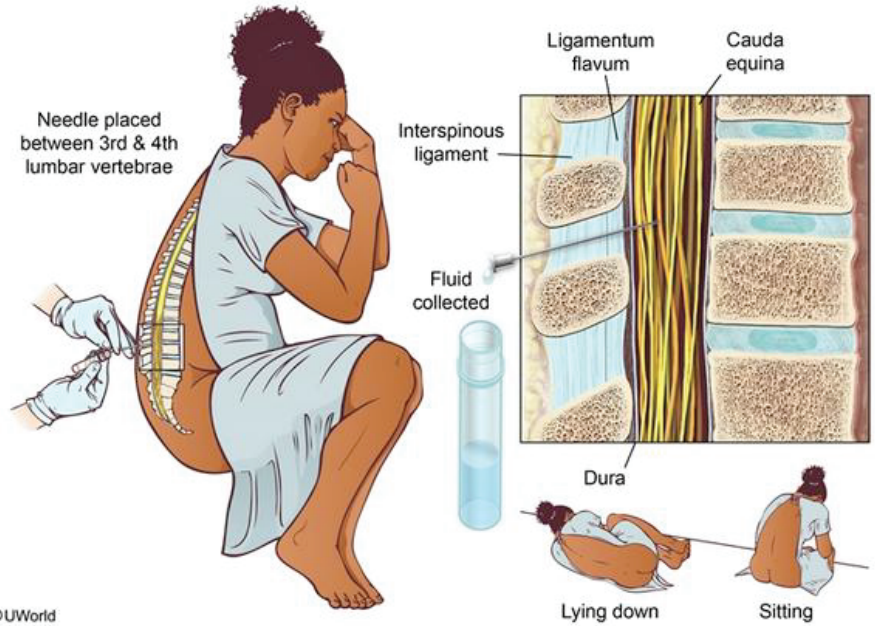
Lumbar puncture

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This patient with fever, headache, delirium, petechial rash, and meningismus likely has meningococcal meningitis. The diagnosis is typically confirmed with lumbar puncture and cerebrospinal fluid (CSF) analysis after neuroimaging excludes a mass lesion.

The spinal cord extends from the medulla to the inferior border of the L1 vertebra in adults (L2/L3 in neonates and infants). The conus medullaris is the tapered lower part of the spinal cord, which subsequently branches out into spinal nerves forming the cauda equina. The pia mater surrounding the spinal cord projects downward to form the filum terminale, which is a filament connecting the conus medullaris to the posterior coccyx. The dura extends below the spinal cord termination level to form a sac containing the CSF, nerve roots, and cauda equina. The dura ends at S2 and fuses with the filum terminale to connect to the coccyx.

**Lumbar puncture** is performed with the patient in the recumbent (preferred for accurate opening pressure measurement) or sitting position. The optimal location for needle insertion is the **L3/L4 or L4/L5 space** as this is well below the spinal cord termination site. The **L4 vertebral body** lies on a line drawn between the highest points of the iliac crests, which can be visually identified and confirmed by palpation.

**(Choice A)** The anterior superior iliac spine is a bony projection of the iliac bone that can be used as a landmark for surface anatomy of the abdomen. This structure serves as the attachment site for the sartorius muscle.


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This patient with fever, headache, delirium, petechial rash, and meningismus likely has meningococcal

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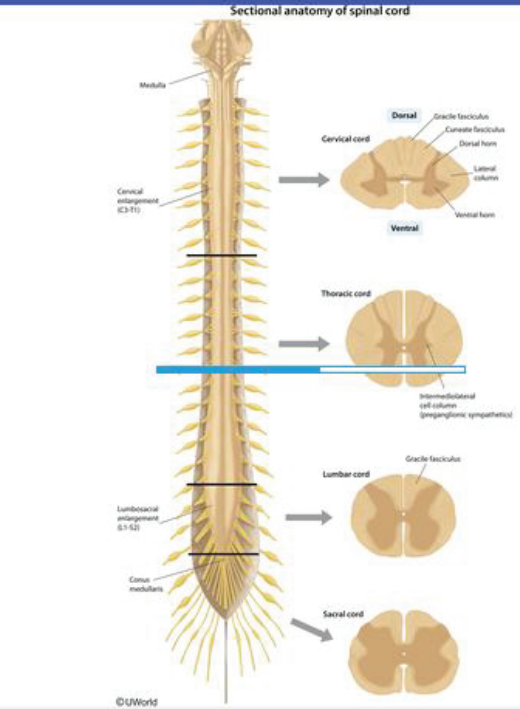


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sarterius muscle



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This patient with fever, headache, delirium, petechial rash, and meningismus likely has meningococcal

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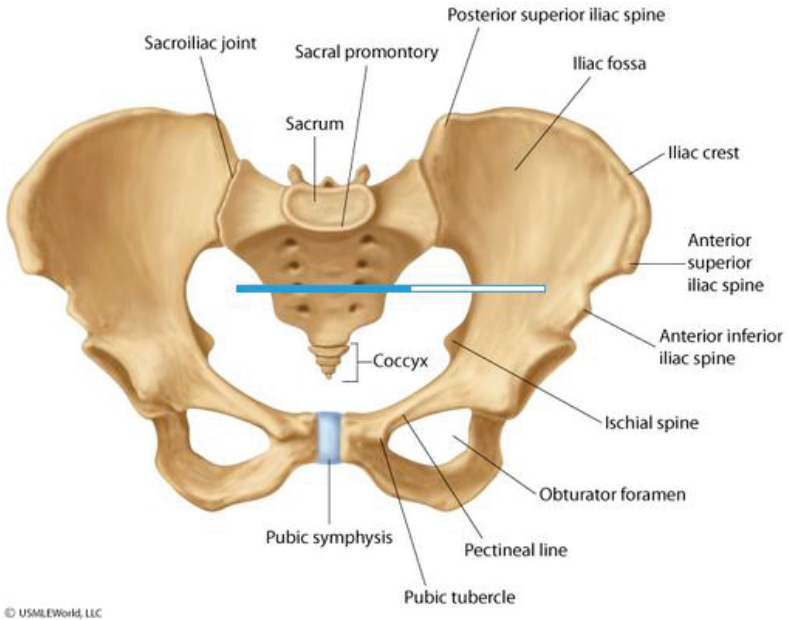
Female pelvis

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sartorius muscle



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**(Choice A)** The anterior superior iliac spine is a bony projection of the iliac bone that can be used as a landmark for surface anatomy of the abdomen. This structure serves as the attachment site for the sartorius muscle.

**(Choice B)** The costal margin is the lower edge of the thorax formed by the anterior ends of the 7th-10th costal cartilages.

**(Choice D)** The inferior angle of the scapula is formed by the medial and lateral borders of the scapula and serves as the origin of the teres major muscle. This scapular region aligns with the spinous processes of T7/T8.

**(Choice E)** The posterior superior iliac spine is the attachment site for the sacrotuberous and posterior sacroiliac ligaments in the iliac crest. The sacral dimples in the skin overlie the posterior superior iliac spine and correspond to the S2 vertebral level.

**Educational objective:**
The optimal location for needle insertion during a lumbar puncture is the L3/L4 or L4/L5 space as this is well below the spinal cord termination site (L1 in adults). The L4 vertebral body lies on a line drawn between the highest points of the iliac crests.



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A 65-year-old woman comes to the office to discuss pain at the posterior chest wall. She was seen 4 months ago for acute shingles involving a right mid-thoracic dermatome. The patient was not treated at that time because she had a delayed presentation and the lesions were already well-crusted and healing. The skin lesions subsequently cleared completely. However, since then, she has had persistent burning and stabbing pain in the same region that has now become severe. She has tried oral acetaminophen without relief. During discussion of treatment options, the patient says she does not want any systemic medications due to concerns about possible side effects. She is started on topical capsaicin cream, and her pain improves markedly over the next several days. Decreased activity of which of the following neurotransmitters is most likely associated with pain relief in this patient?

A. Acetylcholine
B. Dynorphin
C. Endorphin
D. Glycine
E. Histamine



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A. Acetylcholine
B. Dynorphin
C. Endorphin
D. Glycine
E. Histamine
F. Neuropeptide Y
G. Norepinephrine
H. Substance P


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without relief. During discussion of treatment options, the patient says she does not want any systemic medications due to concerns about possible side effects. She is started on topical capsaicin cream, and her pain improves markedly over the next several days. Decreased activity of which of the following neurotransmitters is most likely associated with pain relief in this patient?

A. ~~Acetylcholine~~ (3%)
B. ~~Dynorphin~~ (2%)
C. ~~Endorphin~~ (2%)
D. ~~Glycine~~ (1%)
E. ~~Histamine~~ (1%)
F. Neuropeptide Y (7%)
G. ~~Norepinephrine~~ (0%)
H. Substance P (79%)

79%
01 min, 24 secs
02/01/2021



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| Drugs for neuropathic pain | |
|---|---|
| **Drug** | **Mechanism of action** |
| Tricyclic antidepressants (eg, amitriptyline, nortriptyline)<br><br>SNRIs (eg, duloxetine) | • ↓ Reuptake of serotonin & norepinephrine<br>• Inhibition of pain signals |
| Anticonvulsants (eg, gabapentin, pregabalin) | • Decreased depolarization of neurons in CNS |
| Opioids | • Activation of central opioid receptors |
| Capsaicin (topical) | • Loss of membrane potential in nociceptive fibers |
| Lidocaine (topical) | • Decreased depolarization of neurons in peripheral nerves |

**CNS** = central nervous system; **SNRIs** = serotonin-norepinephrine reuptake inhibitors.

Shingles is due to reactivation of latent varicella zoster virus in sensory ganglia. It causes a vesicular rash


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**CNS** = central nervous system; **SNRIs** = serotonin-norepinephrine reuptake inhibitors.

Shingles is due to reactivation of latent varicella zoster virus in sensory ganglia. It causes a vesicular rash and acute neuritis due to injury to the nerves. The initial pain fades within a few weeks to months, but a subset of patients will have residual neuropathic pain in the affected dermatome. This pain, termed **postherpetic neuralgia** (PHN), relates to sensitization of afferent nerves in the dorsal horn. It may last several months or longer, and has a burning, stabbing, or gnawing character. PHN is usually managed with tricyclic antidepressants (eg, amitriptyline) or anticonvulsants (eg, gabapentin, pregabalin), but nonsystemic options for PHN include lidocaine patches or topical capsaicin.

**Capsaicin** is an irritant found in the chili pepper family. It causes excessive activation of TRPV1 (a transmembrane cation channel), causing a buildup of intracellular calcium that results in long-lasting dysfunction of nociceptive nerve fibers (**defunctionalization**). In addition, capsaicin causes release and subsequent **depletion of substance P**, a polypeptide neurotransmitter involved in transmission of pain signals. On initial application, topical capsaicin causes burning, stinging, and erythema, but persistent exposure leads to a moderate reduction in pain over time.

**(Choices A, D, E, and G)** Capsaicin does not achieve its analgesic effect by acting on these neurotransmitters.


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exposure leads to a moderate reduction in pain over time.

**(Choices A, D, E, and G)** Capsaicin does not achieve its analgesic effect by acting on these neurotransmitters.

**(Choices B and C)** Endorphins and dynorphins are endogenous opioid peptides that achieve their pain-relieving effects by activating μ-opioid and κ-opioid receptors, respectively. Capsaicin does not affect the opioid system.

**(Choice F)** Neuropeptide Y (NPY) is a polypeptide neurotransmitter found in the central and autonomic nervous systems. It is thought to play a role in appetite and pain perception. NPY antagonists have been investigated as potential antiobesity drugs.

**Educational objective:**
Topical capsaicin causes defunctionalization of afferent pain fibers and depletion of substance P. Initial application results in a burning and stinging sensation, but chronic exposure leads to reduced pain transmission.

**References**

- Diagnosing and managing postherpetic neuralgia.
- Topical capsaicin for pain management: therapeutic potential and mechanisms of action of the new



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A 24-year-old man comes to the physician due to excessive daytime sleepiness. The patient is a college student whose symptoms started around age 12, when he began needing more sleep than his peers to feel refreshed. Two years later, he started having daily episodes of sudden weakness, consistently triggered by laughter or crying, in which his head would nod or his knees would buckle for about 30 seconds. The patient also describes times when he was unable to move for several minutes after awakening from sleep. He mentions nightly dreams that seem very real, often featuring activities that he had been engaged in during the preceding day. If measured, which of the following compounds is most likely to be abnormal in this patient's cerebrospinal fluid?

A. 5-hydroxyindoleacetic acid
B. 14-3-3 protein
C. Homovanillic acid
D. Hypocretin-1
E. Melatonin



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student whose symptoms started around age 12, when he began needing more sleep than his peers to feel refreshed. Two years later, he started having daily episodes of sudden weakness, consistently triggered by laughter or crying, in which his head would nod or his knees would buckle for about 30 seconds. The patient also describes times when he was unable to move for several minutes after awakening from sleep. He mentions nightly dreams that seem very real, often featuring activities that he had been engaged in during the preceding day. If measured, which of the following compounds is most likely to be abnormal in this patient's cerebrospinal fluid?

A. ~~5-hydroxyindoleacetic acid~~ (5%)

B. ~~14-3-3 protein~~ (2%)

C. ~~Homovanillic acid~~ (5%)

✓ D. Hypocretin-1 (70%)

✗ E. Melatonin (15%)

Incorrect
Correct answer

70%

01 min, 39 secs

02/14/2021



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| Narcolepsy | |
|---|---|
| **DSM-5 diagnostic criteria** | • Recurrent lapses into sleep or naps (≥3 times/week for 3 months)<br>• ≥1 of the following:<br>◦ Cataplexy: Brief loss of muscle tone precipitated by strong emotion (eg, laughter, excitement)<br>◦ Low cerebrospinal fluid levels of hypocretin-1<br>◦ Shortened REM sleep latency |
| **Associated features** | • Hypnagogic or hypnopompic hallucinations<br>• Sleep paralysis |

This patient's excessive **daytime sleepiness**, episodic loss of motor tone triggered by emotion (**cataplexy**), and inability to move on awakening (**sleep paralysis**) are highly suggestive of **narcolepsy**. Narcolepsy with cataplexy is most often caused by the lack of 2 related neuropeptides: **hypocretin-1** (orexin-A) and **hypocretin-2** (orexin-B), which are produced in neurons located in the lateral hypothalamus. These neuropeptides promote wakefulness and inhibit REM sleep–related phenomena. Hypocretin-1 levels are low to absent in the cerebrospinal fluid (CSF) of patients who have narcolepsy with


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Hypocretin-1 levels are low to absent in the cerebrospinal fluid (CSF) of patients who have narcolepsy with cataplexy.

**(Choice A)** Low CSF 5-hydroxyindoleacetic acid (a metabolite of serotonin) concentration has been associated with impulsive, destructive behaviors, particularly aggression, suicide, and violence.

**(Choice B)** Detection of elevated amounts of 14-3-3 protein in CSF is helpful in diagnosing Creutzfeldt-Jakob disease, a neurodegenerative disease caused by prions.

**(Choice C)** Altered levels of the primary dopamine metabolite, homovanillic acid, have been linked to many psychiatric conditions, including substance use disorders, psychosis, and mood disorders. CSF concentrations of homovanillic acid are also decreased in patients with Parkinson disease.

**(Choice E)** The level of melatonin in CSF has been shown to decrease with the progression of Alzheimer disease.

**Educational objective:**
Hypocretin-1 (orexin-A) and hypocretin-2 (orexin-B) are neuropeptides produced in the lateral hypothalamus that promote wakefulness and inhibit REM sleep–related phenomena. Most patients who have narcolepsy with cataplexy have undetectable levels of hypocretin-1 in their cerebrospinal fluid.

**References**


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A 36-year-old woman is evaluated for several months of tingling and numbness of the right hand and fingers that has progressed to dull, aching pain. The symptoms initially were intermittent but have become persistent, with the pain worsening overnight. The patient works as an office secretary and has had difficulty typing and holding the phone due to hand weakness. On examination, she has weakness of thumb opposition and atrophy of the thenar eminence. The patient attempted treatment with conservative measures but had no significant improvement and has now been referred for surgery. During surgery, incision of which of the following structures is most likely to improve this patient's symptoms?

A. Fibrous flexor sheaths
B. Flexor carpi ulnaris aponeurosis
C. Palmar aponeurosis
D. Synovial sheaths of flexor tendons
E. Transverse carpal ligament

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A. Fibrous flexor sheaths (9%)
B. Flexor carpi ulnaris aponeurosis (2%)
C. Palmar aponeurosis (10%)
D. Synovial sheaths of flexor tendons (3%)
E. Transverse carpal ligament (73%)

73% 19 secs 03/08/2021



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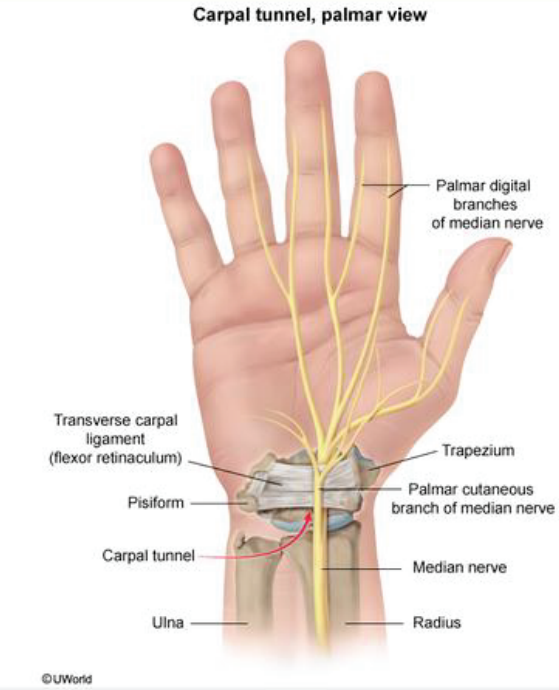


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This patient has right hand pain and numbness, thenar atrophy, and weakness of thumb opposition characteristic of **carpal tunnel syndrome** (CTS). The carpal tunnel is an anatomic space in the wrist between the carpal bones and the **transverse carpal ligament** (flexor retinaculum). The **median nerve** and 9 tendons (eg, flexor digitorum superficialis and profundus, flexor pollicis longus) pass through the carpal tunnel to enter the hand. CTS occurs when **increased pressure** within the carpal tunnel (eg, compression, inflammation) causes median nerve damage.

Often, CTS can be managed successfully with nonsurgical treatments (eg, wrist splint, glucocorticoid injection). However, patients with significant impairment and evidence of median nerve injury on electromyography are often treated with **surgical decompression**. A longitudinal incision through the transverse carpal ligament decreases the pressure on the median nerve, improving patients' symptoms.

**(Choice A)** The fibrous flexor sheaths are thick tunnels on the palmar surface of the fingers that act like pulleys to allow the flexor digitorum profundus tendons to flex the fingers at the interphalangeal joints. Swelling of the tendon and/or fibrous sheath can result in painful catching or locking of the affected finger during flexion (ie, trigger finger).

**(Choice B)** The flexor carpi ulnaris aponeurosis spans from the olecranon to the medial epicondyle and



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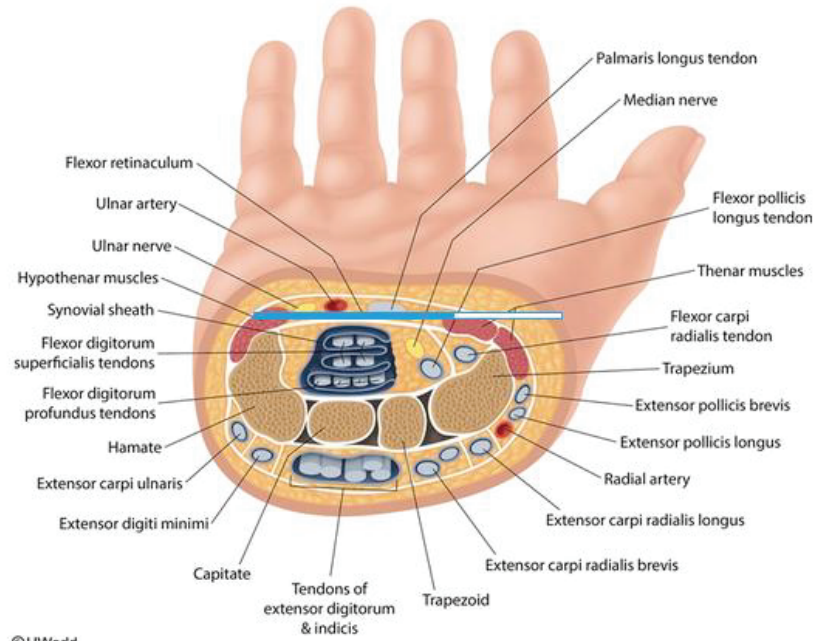
Transverse cross section of wrist & carpal tunnel

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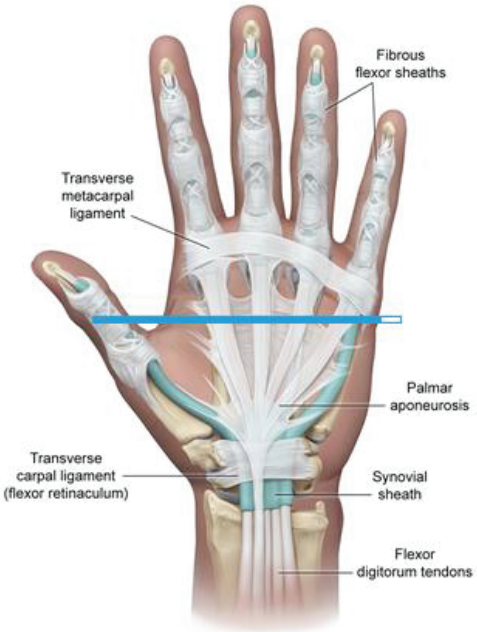
Hand and finger fascia

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**(Choice B)** The flexor carpi ulnaris aponeurosis spans from the olecranon to the medial epicondyle and forms the roof of the cubital tunnel. The ulnar nerve runs through this space, and compression here can cause sensory loss over the ulnar aspect of the hand.

**(Choice C)** The palmar aponeurosis (palmar fascia) spans from the flexor retinaculum at the wrist and is continuous with the fibrous flexor sheaths of the digits. Fibrosis of the palmar aponeurosis can result in Dupuytren contracture, which is a progressive disorder characterized by nodular lesions in the palm with restricted finger motion.

**(Choice D)** The synovial sheaths of the flexor digitorum superficialis and profundus tendons pass through the carpal tunnel around the flexor tendons. However, incision of synovial sheaths would not relieve the pressure on the median nerve in CTS.

**Educational objective:**

The carpal tunnel is formed by the carpal bones and the transverse carpal ligament (flexor retinaculum). Carpal tunnel syndrome results from compression of the median nerve as it passes through the carpal tunnel with 9 flexor tendons. Longitudinal incision of the transverse carpal ligament can decrease pressure within the carpal tunnel, improving patients' symptoms.

**References**



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**(Choice B)** The flexor carpi ulnaris aponeurosis spans from the olecranon to the medial epicondyle and

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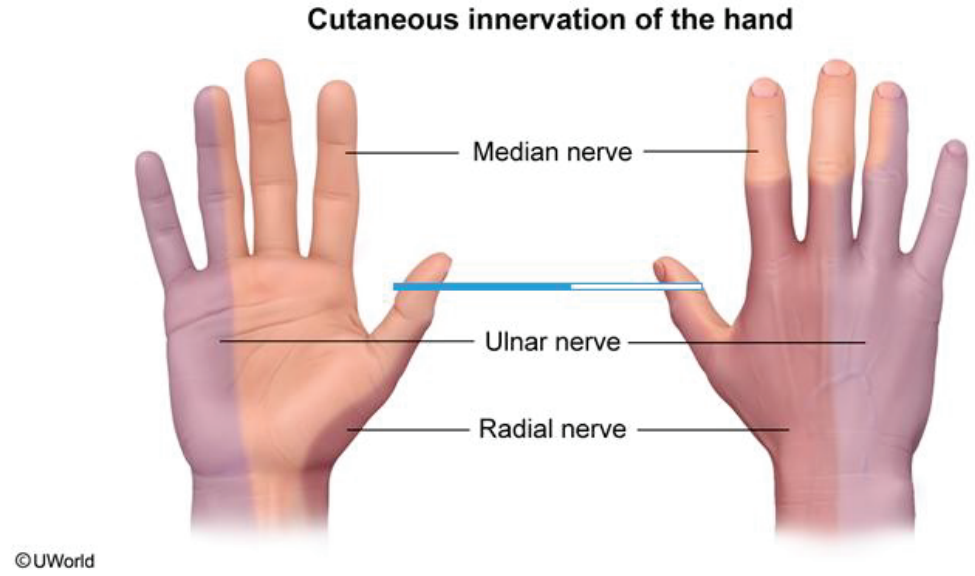


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A 65-year-old man is brought to the emergency department due to acute onset of a severe headache and dizziness. He describes it as a throbbing that localizes to the back of his head, with associated vertigo and mild nausea. The patient has a past medical history of type 2 diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and a recent diagnosis of lung adenocarcinoma. He has smoked 1-2 packs of cigarettes daily for the past 30 years. His temperature is 36.7 C (98 F), blood pressure is 170/96 mm Hg, pulse is 80/min, and respirations are 14/min. Noncontrast head CT reveals an acute hemorrhage in the cerebellar vermis without mass effect or midline shift. Which of the following neurologic findings is most likely to be present during this patient's physical examination?

A. Complete ptosis
B. Dysphagia
C. Hemiparesis
D. Limb dysmetria
E. Resting tremor
F. Truncal ataxia



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mild nausea. The patient has a past medical history of type 2 diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and a recent diagnosis of lung adenocarcinoma. He has smoked 1-2 packs of cigarettes daily for the past 30 years. His temperature is 36.7 C (98 F), blood pressure is 170/96 mm Hg, pulse is 80/min, and respirations are 14/min. Noncontrast head CT reveals an acute hemorrhage in the cerebellar vermis without mass effect or midline shift. Which of the following neurologic findings is most likely to be present during this patient's physical examination?

A. ~~Complete ptosis~~ (1%)
B. ~~Dysphagia~~ (0%)
C. ~~Hemiparesis~~ (1%)
D. ~~Limb dysmetria~~ (8%)
E. Resting tremor (1%)
✓ F. Truncal ataxia (85%)

Correct

85%
01 min, 41 secs
11/14/2020



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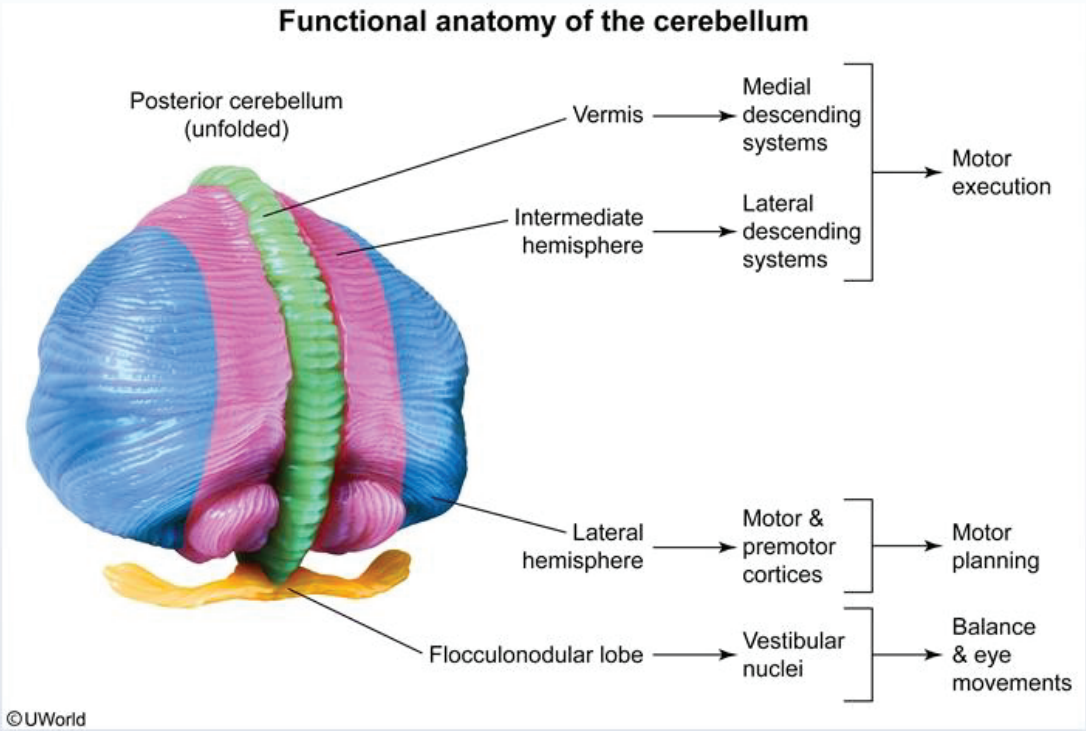


The **cerebellar vermis** modulates axial/truncal posture and coordination via connections with the **medial** descending motor systems (eg, anterior corticospinal, reticulospinal, vestibulospinal, and tectospinal


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The **cerebellar vermis** modulates axial/truncal posture and coordination via connections with the **medial** descending motor systems (eg, anterior corticospinal, reticulospinal, vestibulospinal, and tectospinal tracts). Consequently, acute lesions to this region (eg, due to hemorrhage) typically result in **truncal ataxia**, characterized by a wide-based, unsteady gait. Patients may also develop **vertigo and nystagmus** due to involvement of the inferior vermis and the flocculonodular lobe (vestibulocerebellum), which modulate balance and ocular movements via connections with the vestibular nuclei and medial longitudinal fasciculus.

Other features of cerebellar hemorrhage include nausea and occipital headache. Most cases are caused by hypertensive vasculopathy, but this patient's recent diagnosis of lung adenocarcinoma should also raise concern for hemorrhagic metastasis.

**(Choice A)** Complete ptosis from central lesions may result from injury to the oculomotor nerve fibers within the upper midbrain and is typically associated with contralateral hemiparesis due to adjacent corticospinal tract involvement (eg, Weber syndrome).

**(Choice B)** Oropharyngeal dysphagia is usually associated with lesions in the brainstem due to involvement of cranial nerves IX, X, and XII, and/or their nuclei. Cerebral cortical and subcortical lesions



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**(Choice B)** Oropharyngeal dysphagia is usually associated with lesions in the brainstem due to involvement of cranial nerves IX, X, and XII, and/or their nuclei. Cerebral cortical and subcortical lesions affecting the descending corticobulbar tracts may also lead to oropharyngeal dysphagia.

**(Choice C)** Hemiparesis results from lesions affecting the corticospinal tracts in the cerebral subcortical white matter and brainstem. Cerebellar lesions do not cause pyramidal tract signs or hemiparesis.

**(Choice D)** Limb dysmetria (overshoot/undershoot during targeted movement) is usually associated with lesions affecting the cerebellar hemispheres due to involvement of the **lateral** descending motor systems (eg, lateral corticospinal tract, rubrospinal tract). Hemispheric cerebellar lesions may also cause tremor during goal-directed activity (intention tremor).

**(Choice E)** Resting tremor is typically associated with parkinsonism due to damage of the substantia nigra and its projections to the striatum. Rubral tremor occurs at rest and during goal-directed activity and is associated with combined lesions to the midbrain, substantia nigra, and superior cerebellar peduncle due to disruption of cerebellothalamic pathways.

**Educational objective:**
Acute lesions to the cerebellar vermis typically cause truncal and gait ataxia due to impaired modulation of


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**(Choice C)** Hemiparesis results from lesions affecting the corticospinal tracts in the cerebral subcortical white matter and brainstem. Cerebellar lesions do not cause pyramidal tract signs or hemiparesis.

**(Choice D)** Limb dysmetria (overshoot/undershoot during targeted movement) is usually associated with lesions affecting the cerebellar hemispheres due to involvement of the **lateral** descending motor systems (eg, lateral corticospinal tract, rubrospinal tract). Hemispheric cerebellar lesions may also cause tremor during goal-directed activity (intention tremor).

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**Educational objective:**

Acute lesions to the cerebellar vermis typically cause truncal and gait ataxia due to impaired modulation of the medial-descending motor systems. Involvement of the lower vermis and the flocculonodular lobe also causes vertigo/nystagmus due to dysregulation of the vestibular nuclear complex.

**References**

- Alternating skew deviation due to hemorrhage in the cerebellar vermis.



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A 45-year-old woman is evaluated for numbness and painful tingling of the right hand. The symptoms began 2 months ago and are especially prominent after she plays tennis. On examination, there is diminished sensation in the lateral palm, thenar eminence, and palmar aspect of the first 3½ digits of the right hand. This patient most likely has an injury involving a nerve that courses between which of the following structures?

A. Biceps and coracobrachialis muscles
B. Flexor carpi ulnaris and flexor digitorum profundus muscles
C. Humeral and ulnar heads of the pronator teres muscle
D. Olecranon and the medial epicondyle of the humerus
E. Supinator muscle and the head of the radius

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A 45-year-old woman is evaluated for numbness and painful tingling of the right hand. The symptoms began 2 months ago and are especially prominent after she plays tennis. On examination, there is diminished sensation in the lateral palm, thenar eminence, and palmar aspect of the first 3½ digits of the right hand. This patient most likely has an injury involving a nerve that courses between which of the following structures?

A. Biceps and coracobrachialis muscles (9%)

B. Flexor carpi ulnaris and flexor digitorum profundus muscles (25%)

✓ C. Humeral and ulnar heads of the pronator teres muscle (29%)

D. ~~Olecranon and the medial epicondyle of the humerus~~ (13%)

E. ~~Supinator muscle and the head of the radius~~ (21%)

Correct

29%
Answered correctly

14 mins, 34 secs
Time Spent

09/22/2020
Last Updated



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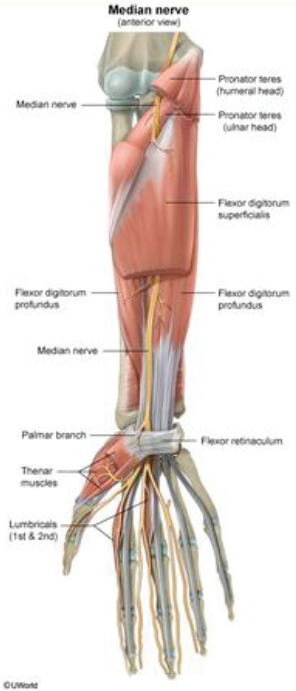


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This patient has diminished sensation that involves the entire sensory distribution of the median nerve and is exacerbated by repetitive, forceful pronation (eg, tennis). This presentation is most consistent with compression of the median nerve as it passes between the two heads of the pronator teres (ie, pronator teres syndrome).

The median nerve arises from the medial and lateral cords of the brachial plexus and travels with the brachial artery in the medial bicipital groove (ie, longitudinal hollow between the biceps brachii and triceps brachii muscles) of the upper arm. In the forearm, the median nerve **courses between** the humeral and ulnar **heads of the pronator teres muscle** and between the flexor digitorum superficialis and flexor digitorum profundus muscles before entering the hand through the carpal tunnel.

Median nerve **compression at the carpal tunnel**, which is distal to the takeoff of the palmar branch, typically **impairs sensation** to the palmar aspects of the **first 3½ digits**. In contrast, **compression by the pronator teres** occurs proximal to the takeoff of the palmar branch; therefore, sensation is impaired not only to the palmar aspect of the first 3½ digits but also to the **entire lateral palm** and thenar eminence (ie, sensory distribution of the palmar branch).

**(Choice A)** The musculocutaneous nerve courses between the biceps brachii and coracobrachialis


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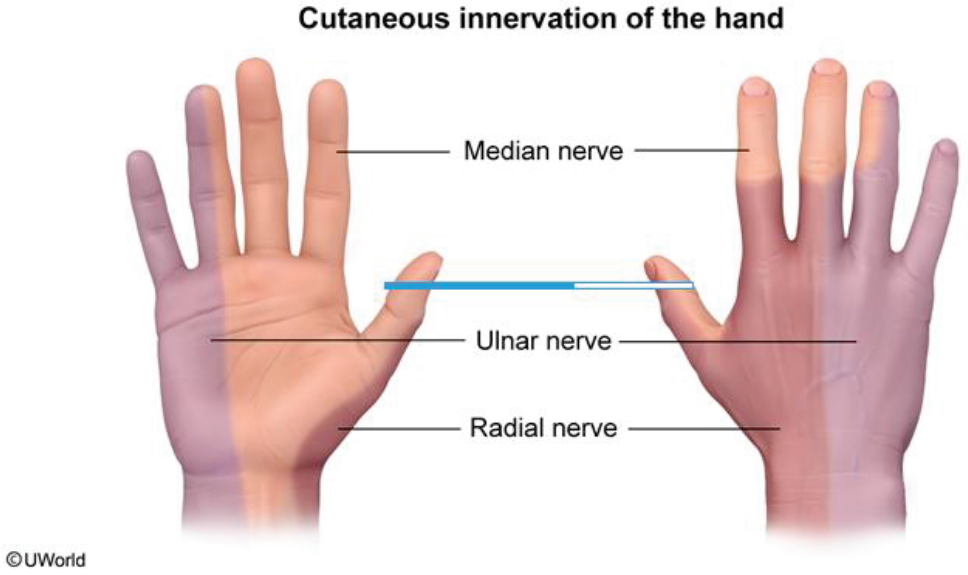


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(Choice A) The musculocutaneous nerve courses between the biceps brachii and coracobrachialis



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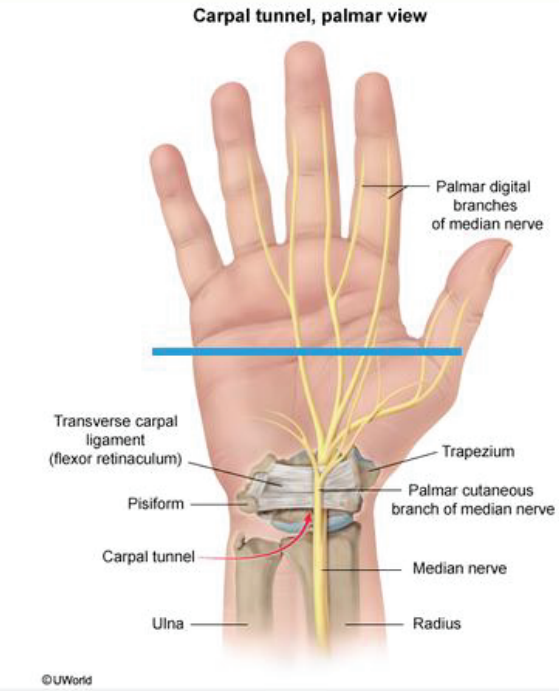


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(Choice A) The musculocutaneous nerve courses between the biceps brachii and coracobrachialis



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**(Choice A)** The musculocutaneous nerve courses between the biceps brachii and coracobrachialis muscles in the upper arm. Injury (eg, trauma, shoulder dislocation) can cause sensory loss over the lateral forearm.

**(Choices B and D)** The ulnar nerve courses between the olecranon and the medial epicondyle of the humerus (ie, the cubital tunnel) before passing between the flexor carpi ulnaris and flexor digitorum profundus muscles in the forearm. Ulnar nerve injury at the elbow (eg, compression, trauma) can cause sensory loss in the dorsomedial hand, medial palm, and medial 1½ digits.

**(Choice E)** The deep branch of the radial nerve (ie, posterior interosseous nerve) courses between the supinator muscle and the head of the radius in the upper forearm. Injury (eg, humeral fracture, compression) can cause sensory loss in the posterior forearm, dorsolateral hand, and dorsal thumb.

**Educational objective:**
In the forearm, the median nerve courses between the humeral and ulnar heads of the pronator teres muscle and between the flexor digitorum superficialis and flexor digitorum profundus muscles. Compression prior to the takeoff of the palmar branch (eg, between the heads of the pronator teres) results in sensory loss over the lateral palm and palmar aspects of the first 3½ digits.

**References**


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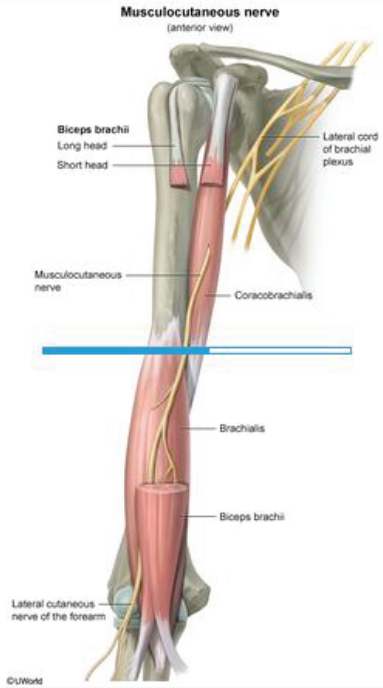


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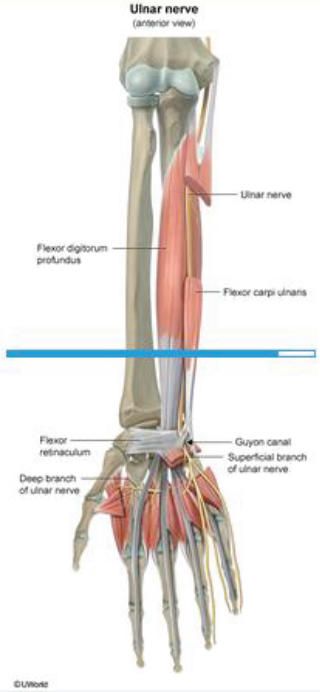


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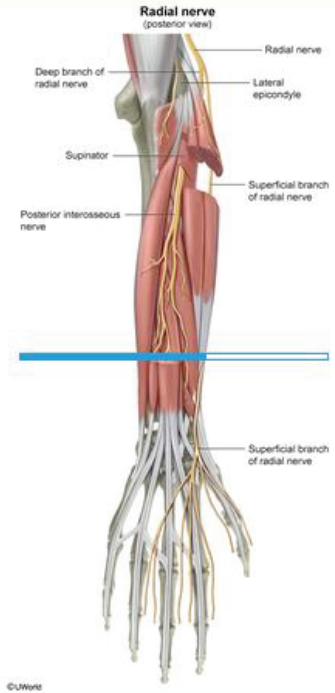


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A 35-year-old woman, gravida 2 para 1, comes to the office for prenatal evaluation. The patient says she had been using condoms for birth control and unintentionally became pregnant. Her last menstrual period was 2 months ago, and home pregnancy tests are positive. She has not been taking prenatal vitamins. The patient has a healthy, 5-year-old daughter who was born after an uneventful pregnancy. She has a history of rheumatoid arthritis, and her joint symptoms are controlled with methotrexate therapy. The patient has no other medical conditions and takes no other medications. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits, and physical examination shows no abnormalities. Serum β-hCG is elevated, and transvaginal ultrasonography shows a normal gestational sac and embryo. This patient's unborn child is at the greatest risk for which of the following congenital defects?

A. Branchial arch anomalies
B. Neural tube defects
C. Renal dysplasia
D. Sacral agenesis
E. Skeletal lesions


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The patient has a healthy, 5-year-old daughter who was born after an uneventful pregnancy. She has a history of rheumatoid arthritis, and her joint symptoms are controlled with methotrexate therapy. The patient has no other medical conditions and takes no other medications. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits, and physical examination shows no abnormalities. Serum β-hCG is elevated, and transvaginal ultrasonography shows a normal gestational sac and embryo. This patient's unborn child is at the greatest risk for which of the following congenital defects?

A. Branchial arch anomalies
B. Neural tube defects
C. Renal dysplasia
D. Sacral agenesis
E. Skeletal lesions
F. Thyroid hypoplasia

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The patient has a healthy, 5-year-old daughter who was born after an uneventful pregnancy. She has a history of rheumatoid arthritis, and her joint symptoms are controlled with methotrexate therapy. The patient has no other medical conditions and takes no other medications. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits, and physical examination shows no abnormalities. Serum β-hCG is elevated, and transvaginal ultrasonography shows a normal gestational sac and embryo. This patient's unborn child is at the greatest risk for which of the following congenital defects?

A. Branchial arch anomalies (2%)
✓ B. Neural tube defects (91%)
C. Renal dysplasia (1%)
D. Sacral agenesis (1%)
E. Skeletal lesions (1%)
F. Thyroid hypoplasia (1%)


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## Folate antagonists

| Mechanism | Drug | Therapeutic applications |
|---|---|---|
| **Inhibition of DHFR** | Methotrexate | • Rheumatoid arthritis<br>• Cancer |
| | Sulfasalazine | • Rheumatoid arthritis<br>• Inflammatory bowel disease |
| | Triamterene | • Diuretic (with HCTZ) for edema & hypertension |
| | Trimethoprim | • Cystitis<br>• *Pneumocystis* pneumonia (with sulfamethoxazole) |
| **Variable inhibition of folate metabolism** | • Valproic acid<br>• Carbamazepine<br>• Phenytoin | • Seizure disorders<br>• Bipolar disorder (valproic acid & carbamazepine) |

**DHFR** = dihydrofolate reductase; **HCTZ** = hydrochlorothiazide.



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DHFR = dihydrofolate reductase, HCTZ = hydrochlorothiazide.

This patient with an unintended pregnancy has been taking **methotrexate**, a disease-modifying antirheumatic drug, to control symptoms of **rheumatoid arthritis**. Methotrexate is a folic acid analog that **competitively inhibits** dihydrofolate reductase, which produces nucleic acid precursors that are essential to DNA synthesis and repair. **Rapidly dividing cells** (eg, neural tube cells, stem cells, hepatic cells, epithelial cells) are **particularly susceptible** to folate antagonism. All patients taking methotrexate should also take a daily folic acid supplement to ameliorate the potential adverse effects (eg, oral ulcers, hepatotoxicity).

Methotrexate and other folate antagonists have **abortifacient** and/or **teratogenic** effects when used during the first trimester. They are contraindicated in pregnant women except under specific circumstances (eg, cancer therapy with no better alternative, treatment of ectopic pregnancy). Adverse effects of methotrexate use to the fetus include cardiovascular, urinary tract, and **neural tube defects** (eg, anencephaly, spina bifida).

**(Choice A)** Under the influence of Hox (homeobox) genes, the branchial arches develop into many head and neck tissues (eg, muscles, bones, and cartilage of the face, neck, and pharynx). Retinoids (eg, topical tretinoin) are vitamin A derivatives used in the treatment of acne that interfere with the Hox signaling pathways. If used during pregnancy, they can cause branchial arch abnormalities (eg, CNS, thymic, and


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DHFR = dihydrofolate reductase; HCTZ = hydrochlorothiazide.

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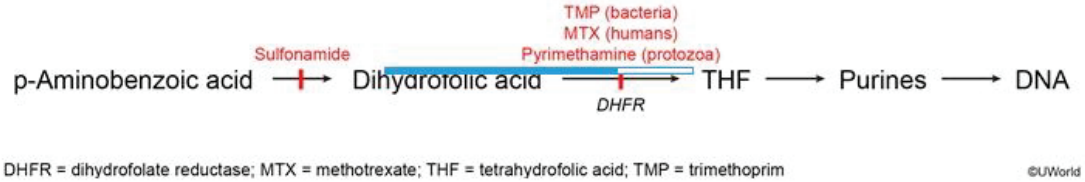


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pathways. If used during pregnancy, they can cause branchial arch abnormalities (eg, CNS, thymic, and



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and neck tissues (eg, muscles, bones, and cartilage of the face, neck, and pharynx). Retinoids (eg, topical tretinoin) are vitamin A derivatives used in the treatment of acne that interfere with the Hox signaling pathways. If used during pregnancy, they can cause branchial arch abnormalities (eg, CNS, thymic, and craniofacial defects).

**(Choice C)** Renal dysplasia can be a complication of second or third trimester fetal exposure to ACE inhibitors in hypertensive mothers. Because fetal renal function is essential to maintain amniotic fluid volume, impaired renal function can lead to pulmonary hypoplasia, limb contractions, growth restriction, or cord compression with poor fetal outcomes.

**(Choice D)** Sacral agenesis (ie, caudal regression syndrome) is a rare malformation that occurs almost exclusively in infants of diabetic mothers. Defects can include incomplete development of the sacrum, lumbar vertebrae, and lower extremities.

**(Choice E)** Skeletal lesions can occur in congenital syphilis infection due to an inflammatory response (eg, periostitis, osteochondritis) to *Treponema pallidum* spirochetes in highly vascular areas of bones (eg, Hutchinson teeth). Although methotrexate exposure can cause skeletal development abnormalities, discrete inflammatory lesions would not be expected.

**(Choice F)** Thyroid hypoplasia is a complication of inadvertent fetal exposure to radioactive iodine (I131)


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Hutchinson teeth

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(Choice F) Thyroid hypoplasia is a complication of inadvertent fetal exposure to radioactive iodine (I131)



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exclusively in infants of diabetic mothers. Defects can include incomplete development of the sacrum, lumbar vertebrae, and lower extremities.

**(Choice E)** Skeletal lesions can occur in congenital syphilis infection due to an inflammatory response (eg, periostitis, osteochondritis) to *Treponema pallidum* spirochetes in highly vascular areas of bones (eg, Hutchinson teeth). Although methotrexate exposure can cause skeletal development abnormalities, discrete inflammatory lesions would not be expected.

**(Choice F)** Thyroid hypoplasia is a complication of inadvertent fetal exposure to radioactive iodine (I131) in patients receiving treatment for hyperthyroidism or thyroid cancer who unintentionally become pregnant.

**Educational objective:**

Methotrexate and other folic acid antagonists adversely affect rapidly dividing cells (eg, epithelial cells, stem cells, neural tube cells) by limiting the production of precursors essential to DNA synthesis and repair. If used in the first trimester of pregnancy, these drugs can cause major congenital abnormalities (eg, cardiovascular abnormalities, neural tube defects).

**References**

- Folic acid antagonists during pregnancy and the risk of birth defects.

Embryology Nervous System Neural tube defects



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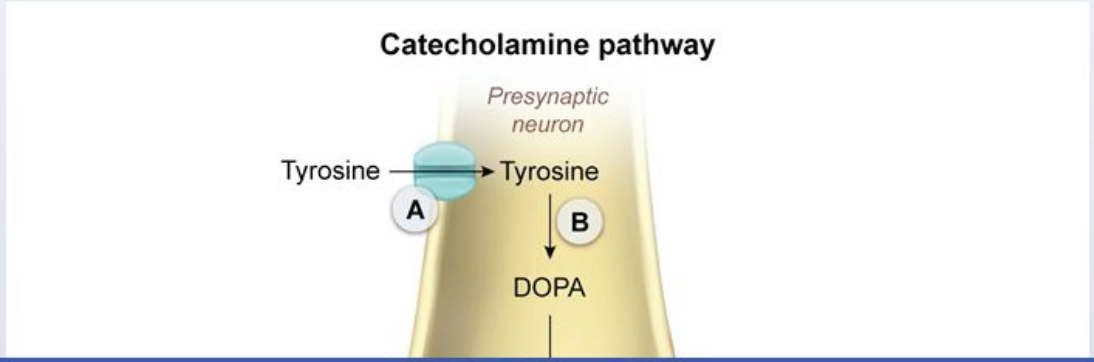
A 55-year-old man comes to the office due to intermittent shortness of breath, cough, and chest tightness over the past 3 months. The patient had asthma as a child that improved in adolescence, and he has not required inhalers or steroids since. He feels that his current symptoms are similar to his prior asthma symptoms. The patient was recently diagnosed with essential tremor, which has improved with medical therapy; he has no other chronic medical conditions. He is a lifetime nonsmoker and does not use alcohol or illicit drugs. Blood pressure is 125/75 mm Hg, pulse is 58/min, and respirations are 16/min. Physical examination reveals bilateral scattered expiratory wheezes. Heart sounds are normal and there is no extremity edema. This patient's symptom recurrence is most likely attributable to a medication that affects which of the following steps?





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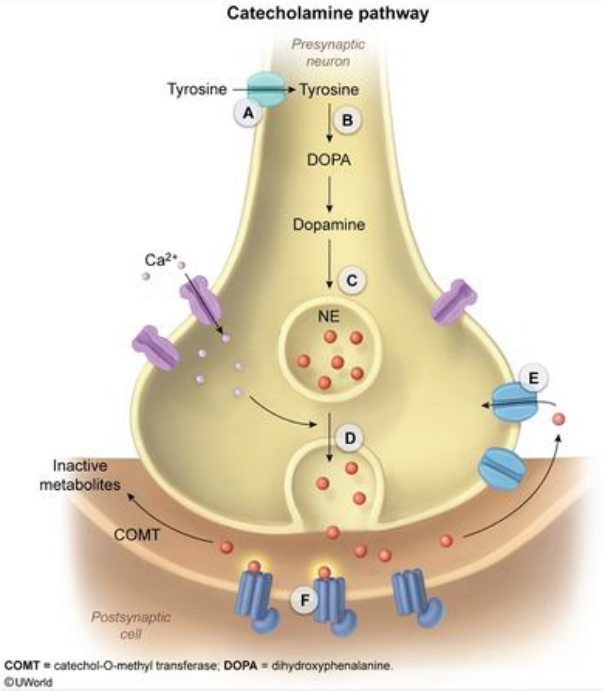


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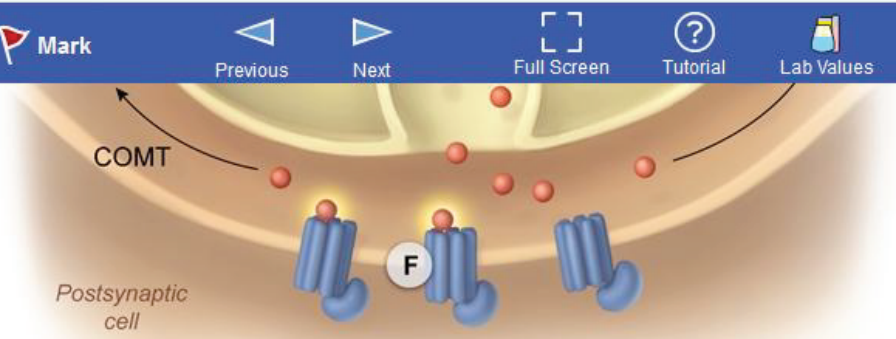


**COMT** = catechol-O-methyl transferase; **DOPA** = dihydroxyphenalanine.

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- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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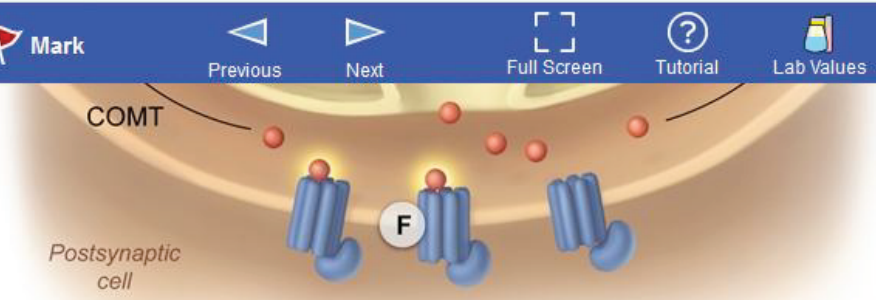


**COMT** = catechol-O-methyl transferase; **DOPA** = dihydroxyphenalanine.
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- A. A (1%)
- B. B (4%)
- ✗ C. C (7%)
- D. D (13%)
- E. E (19%)
- ✓ F. F (53%)

Incorrect
Correct answer

53%
Answered correctly

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| Effects of adrenergic blockade | | | |
|---|---|---|---|
| **Receptor** | **Target organ** | **Effect** | **Potential adverse effects** |
| **B1-adrenergic blockade** | Heart | ↓ Heart rate<br>↓ Contractility<br>↓ $O_2$ consumption | Worsening of heart failure<br>Bradycardia/heart block |
| | Kidney | ↓ Renin release | |
| **B2-adrenergic blockade** | Muscle vasculature | Vasospasm | Exacerbation of peripheral artery disease |
| | Lungs | Bronchoconstriction | Worsening of obstructive lung disease |
| | Liver | ↓ Glycogenolysis & gluconeogenesis | May cause hypoglycemia in diabetic patients |
| | Most tissues | ↓ Potassium entry into cells | Hyperkalemia |


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This patient has developed symptoms of intermittent asthma (eg, cough, wheeze, dyspnea) associated with a new medication for his **essential tremor** (ET). ET is a common movement disorder, and beta blockers are often used as first-line therapy for debilitating or distressful symptoms. Beta blockers prevent the interaction of epinephrine and norepinephrine with receptors at adrenergic synapses; in ET, this is thought to help dampen the sensitivity of muscle spindles, which improves tremor symptoms by smoothing out the force of contraction.

Propranolol, the most commonly used medication for treatment of ET, is a **nonselective beta blocker** (ie, inhibits both beta-1 and beta-2 receptors). In patients with reactive airway diseases (eg, asthma, chronic obstructive pulmonary disease), **inhibition of beta-2 receptors** can cause **bronchoconstriction** with resultant asthma symptoms. Selective beta-1 blockers are often better tolerated in patients with asthma; however, selectivity is dose-dependent and patients can develop bronchoconstriction at high doses.

**(Choice A)** Tyrosine is transported into the cell by the large neutral amino acid transporter.

**(Choice B)** The conversion of tyrosine to dihydroxyphenylalanine (DOPA) by tyrosine hydroxylase is the rate-limiting step in catecholamine biosynthesis. This enzyme was previously inhibited by drugs used to treat pheochromocytoma, but these are no longer used due to a poor side effect profile.

**(Choice C)** The medication reserpine inhibits vesicular monoamine transporter, thereby inhibiting


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**(Choice C)** The medication reserpine inhibits vesicular monoamine transporter, thereby inhibiting dopamine entry into presynaptic vesicles and essentially causing a chemical sympathectomy. Reserpine is occasionally used as an antipsychotic. It may cause wheezing in some patients but is not indicated in the treatment of ET.

**(Choice D)** Adrenergic neuron blockers such as guanethidine inhibit norepinephrine release, lowering blood pressure and heart rate. Guanethidine is occasionally used for chronic pain syndrome but does not cause bronchoconstriction; it is not used in management of ET.

**(Choice E)** Tricyclic antidepressants and cocaine work by inhibiting norepinephrine reuptake by presynaptic neurons. These agents can worsen symptoms in ET.

**Educational objective:**
Beta blockers are used in the treatment of essential tremor. Propranolol, a nonselective beta blocker, is the most commonly used therapy and prevents the interaction of epinephrine and norepinephrine with beta-1 and beta-2 receptors to relieve tremor symptoms. However, inhibition of pulmonary beta-2 receptors in patients with underlying reactive airway disease can cause bronchoconstriction, leading to cough, wheeze, and dyspnea.


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A 28-year-old woman with a history of type 1 diabetes mellitus comes to the hospital due to abdominal pain, nausea, and vomiting. She is found to have severe hyperglycemia, high anion gap metabolic acidosis, and an elevated beta-hydroxybutyrate level. While being evaluated in the emergency department, the patient develops involuntary, rhythmic jerking of her right upper extremity that lasts for about a minute. She remains fully alert during and after the event. The patient has never had similar symptoms in the past and has no other medical conditions. Physical examination shows no weakness or sensory loss in the right upper extremity. Which of the following is the most likely diagnosis?

- A. Acute dystonia
- B. Focal onset seizure
- C. Generalized absence seizure
- D. Generalized tonic-clonic seizure
- E. Hemiballism
- F. Tic disorder


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pain, nausea, and vomiting. She is found to have severe hyperglycemia, high anion gap metabolic acidosis, and an elevated beta-hydroxybutyrate level. While being evaluated in the emergency department, the patient develops involuntary, rhythmic jerking of her right upper extremity that lasts for about a minute. She remains fully alert during and after the event. The patient has never had similar symptoms in the past and has no other medical conditions. Physical examination shows no weakness or sensory loss in the right upper extremity. Which of the following is the most likely diagnosis?

- A. Acute dystonia (7%)
- ✓ B. Focal onset seizure (74%)
- C. Generalized absence seizure (0%)
- D. Generalized tonic-clonic seizure (1%)
- E. Hemiballism (15%)
- F. Tic disorder (1%)

Correct

74%

01 min, 01 sec

03/07/2021



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| Seizure type | Description | Preferred anticonvulsants |
|---|---|---|
| **Focal onset** (involves a single cerebral hemisphere at onset) | | |
| **Aware** | • No loss of consciousness or postictal state<br>• Motor, sensory, autonomic, or cognitive symptoms | • Carbamazepine*<br>• Lamotrigine<br>• Levetiracetam<br>• Phenytoin* |
| **Impaired awareness** | • Appears awake but consciousness is altered (eg, blank stare)<br>• Postictal state<br>• May have automatisms (eg, lip smacking) | |
| **Generalized onset** (involves both hemispheres at onset) | | |
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state | |


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| | | |
|---|---|---|
| | followed by rhythmic jerking (clonic) | • Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |
| **Absence** | • Brief episodes of altered consciousness (eg, blank stare)<br>• May have automatisms<br>• Usually no postictal state | • Ethosuxamide<br>• Valproic acid |

*Narrow-spectrum agents can also treat focal-onset seizures that evolve into bilateral tonic-clonic seizures.

This patient with abdominal pain, vomiting, hyperglycemia, anion gap metabolic acidosis, and elevated beta-hydroxybutyrate has diabetic ketoacidosis. **Metabolic derangements** (eg, hyperglycemia, acidosis) in patients with **diabetic ketoacidosis** may cause neurologic dysfunction manifesting as altered mental status, focal neurologic deficits, and/or seizure.

**Seizures** occur due to abnormal, synchronous discharges of neurons in the cerebral cortex. They are classified as either **focal onset** (previously known as partial) if they originate from a localized region of **one cerebral hemisphere** or generalized if they involve both hemispheres at onset. Focal seizures can be


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| Anion gap metabolic acidosis | |
|---|---|
| **Calculation** | Anion gap = sodium – (chloride + bicarbonate)<br>(Normal: 10-14) |
| **Common causes**<br>Mnemonic: MUDPILES | • Methanol<br>• Uremia<br>• Diabetic ketoacidosis<br>• Propylene glycol/paraldehyde<br>• Isoniazid/iron<br>• Lactic acidosis<br>• Ethylene glycol (antifreeze)<br>• Salicylates (aspirin) |

| | |
|---|---|
| **Myoclonic** | |
| **Absence** | |

*Narrow-spectrum

This patient with ab
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status, focal neurologic deficits, and/or seizure.

**Seizures** occur due to abnormal, synchronous discharges of neurons in the cerebral cortex. They are classified as either **focal onset** (previously known as partial) if they originate from a localized region of **one cerebral hemisphere** or generalized if they involve both hemispheres at onset. Focal seizures can be subclassified based on level of consciousness:

- Focal seizures with retained awareness (previously known as simple partial): Patients remain awake and interactive.
- Focal seizures with impaired awareness (previously known as complex partial): Patients appear awake but do not interact appropriately (eg, blank stare). Postictal state (eg, confusion, sedation) is common.

The manifestations of focal seizure depend on the brain region in which the seizure activity is occurring. This patient's episodic right upper limb rhythmic jerking suggests a **focal seizure with retained awareness** originating in the contralateral motor cortex.

**(Choice A)** Acute dystonia is a sustained, involuntary muscle contraction with abnormal posturing (eg, torticollis); it often occurs after exposure to dopamine antagonists (eg, haloperidol). Rhythmic jerking is more consistent with seizure activity.


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**(Choice C)** Generalized absence seizure involves both hemispheres at onset and presents as a brief (<10 sec) staring spell with impaired consciousness. It typically occurs in children, and patients may have hundreds of episodes a day.

**(Choice D)** Generalized tonic-clonic seizure is characterized by loss of consciousness with diffuse, bilateral muscle contractions of the limbs followed by rhythmic jerking. Associated features may include tongue biting and urinary/bowel incontinence.

**(Choice E)** Hemiballism is characterized by involuntary, unilateral, nonrhythmic, wide-amplitude movements of the extremities (eg, arm flailing). It often occurs with Huntington chorea, an autosomal dominant disease that also causes psychiatric symptoms and dementia.

**(Choice F)** Motor tics are sudden, brief movements that may include arm jerking but are characterized by an overwhelming urge to perform the movement followed by feelings of relief. They can be voluntarily suppressed for brief periods.

**Educational objective:**
Seizures are classified as either focal onset if they originate from a localized region of one cerebral hemisphere or generalized if they involve both hemispheres at onset. Focal seizures can be subclassified as retained awareness (patients remain interactive) or impaired awareness (patients appear awake but do


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**(Choice D)** Generalized tonic-clonic seizure is characterized by loss of consciousness with diffuse, bilateral muscle contractions of the limbs followed by rhythmic jerking. Associated features may include tongue biting and urinary/bowel incontinence.

**(Choice E)** Hemiballism is characterized by involuntary, unilateral, nonrhythmic, wide-amplitude movements of the extremities (eg, arm flailing). It often occurs with Huntington chorea, an autosomal dominant disease that also causes psychiatric symptoms and dementia.

**(Choice F)** Motor tics are sudden, brief movements that may include arm jerking but are characterized by an overwhelming urge to perform the movement followed by feelings of relief. They can be voluntarily suppressed for brief periods.

**Educational objective:**
Seizures are classified as either focal onset if they originate from a localized region of one cerebral hemisphere or generalized if they involve both hemispheres at onset. Focal seizures can be subclassified as retained awareness (patients remain interactive) or impaired awareness (patients appear awake but do not interact appropriately). Manifestations of focal seizure depend on the brain region in which the seizure activity occurs.

**References**


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A 58-year-old man comes to the emergency department due to sudden right-sided weakness. He has no sensory loss, problems speaking/swallowing, or difficulty with balance. The patient was previously told that he has elevated blood pressure, but he does not routinely follow up with his physician. He takes no medications. Examination shows intact cranial nerves and sensory function. The patient has 3/5 muscle strength on the right side. Initial CT scan without contrast reveals no abnormalities. Four weeks later, repeat brain imaging shows a 9-mm, fluid-filled cavitary lesion in the left internal capsule. This patient's condition is most likely caused by which of the following?

A. Cardiac embolism
B. Carotid artery atherosclerosis
C. Hypertensive arteriolar sclerosis
D. Hypertensive encephalopathy
E. Hypoxic encephalopathy
F. Saccular aneurysm



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sensory loss, problems speaking/swallowing, or difficulty with balance. The patient was previously told that he has elevated blood pressure, but he does not routinely follow up with his physician. He takes no medications. Examination shows intact cranial nerves and sensory function. The patient has 3/5 muscle strength on the right side. Initial CT scan without contrast reveals no abnormalities. Four weeks later, repeat brain imaging shows a 9-mm, fluid-filled cavitary lesion in the left internal capsule. This patient's condition is most likely caused by which of the following?

A. Cardiac embolism (6%)
B. Carotid artery atherosclerosis (5%)
C. Hypertensive arteriolar sclerosis (54%)
D. ~~Hypertensive encephalopathy~~ (12%)
E. ~~Hypoxic encephalopathy~~ (3%)
F. ~~Saccular aneurysm~~ (17%)

Correct

54%

02 mins, 27 secs

12/13/2020



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This patient has pure motor hemiparesis and a small cavitary lesion in the **internal capsule**, characteristic of a **lacunar infarct**. This type of stroke affects the **small penetrating arterioles** that supply the deep brain structures (eg, basal ganglia, pons) and subcortical white matter (eg, internal capsule, corona radiata). Lacunar infarcts are primarily associated with chronic hypertension, which promotes lipohyalinosis, microatheroma formation, and hardening/thickening of the vessel wall **(hypertensive arteriolar sclerosis)**. This leads to progressive narrowing of the arteriolar lumen and predisposes to thrombotic vessel occlusion, which causes characteristic clinical syndromes, depending on the portion of the brain affected:

- Posterior limb of the internal capsule and/or basal pons - **pure motor hemiparesis** or ataxia-hemiplegia syndrome (ie, ipsilateral limb ataxia out of proportion to motor deficit)
- Genu/anterior limb of the internal capsule and/or basal pons - dysarthria-clumsy hand syndrome (ie, dysarthria and dysphagia with clumsiness of one hand)
- Ventroposterolateral or ventroposteromedial thalamus - pure sensory stroke

In the acute setting, CT imaging may not reveal the expected hypodensity of ischemic stroke due to the **small infarct size** (usually <15 mm). After several weeks, these necrotic lesions turn into cavitary spaces filled with cerebrospinal fluid and surrounded by scar tissue called lacunas.


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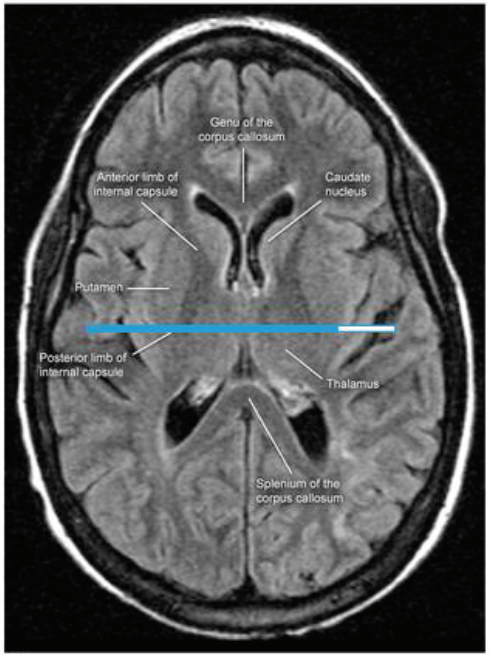
## Exhibit Display

Internal capsule

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filled with cerebrospinal fluid and surrounded by scar tissue called lacunas



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In the acute setting, CT imaging may not reveal the expected hypodensity of ischemic stroke due to the **small infarct size** (usually <15 mm). After several weeks, these necrotic lesions turn into cavitary spaces filled with cerebrospinal fluid and surrounded by scar tissue called lacunas.

**(Choices A and B)** Cardiac embolism and carotid artery atherosclerosis usually result in occlusion of medium to large cerebral vessels (eg, middle cerebral artery), causing large-territory ischemic infarctions of the cerebral cortex evident on CT scan as large areas of hypodensity.

**(Choice D)** Hypertensive encephalopathy is characterized by progressive headache and nausea/vomiting followed by nonlocalizing neurologic symptoms (eg, confusion). Cerebral imaging may be normal or show parietooccipital white matter edema.

**(Choice E)** Hypoxic encephalopathy occurs from global interruption of the cerebral blood supply (eg, due to cardiac arrest). It commonly presents with decreased consciousness (eg, coma, vegetative state) as opposed to focal neurologic deficits. Cerebral imaging may show watershed infarcts at the border of perfusion zones between the major cerebral arteries.

**(Choice F)** Saccular aneurysm rupture is associated with subarachnoid hemorrhage. Patients usually have abrupt onset of severe headache, and CT will show hyperattenuation (hemorrhage) in the sulci and basal cisterns. Focal neurologic deficits are uncommon.



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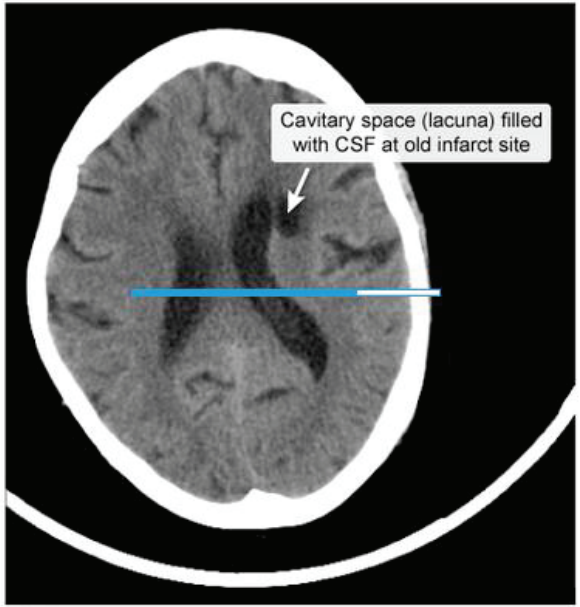
Exhibit Display

Chronic left corona radiata ischemic infarct

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basal cisterns. Focal neurologic deficits are uncommon.



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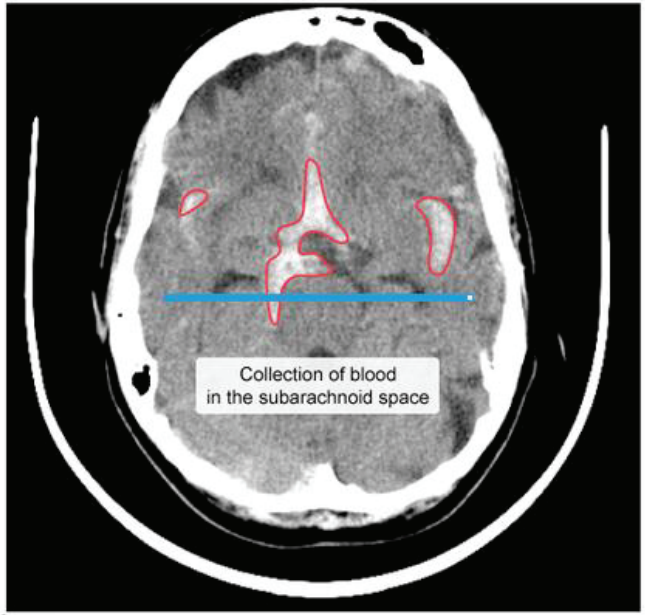
Exhibit Display

Subarachnoid hemorrhage

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basal cisterns. Focal neurologic deficits are uncommon.



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followed by nonlocalizing neurologic symptoms (eg, confusion). Cerebral imaging may be normal or show parietooccipital white matter edema.

**(Choice E)** Hypoxic encephalopathy occurs from global interruption of the cerebral blood supply (eg, due to cardiac arrest). It commonly presents with decreased consciousness (eg, coma, vegetative state) as opposed to focal neurologic deficits. Cerebral imaging may show watershed infarcts at the border of perfusion zones between the major cerebral arteries.

**(Choice F)** Saccular aneurysm rupture is associated with subarachnoid hemorrhage. Patients usually have abrupt onset of severe headache, and CT will show hyperattenuation (hemorrhage) in the sulci and basal cisterns. Focal neurologic deficits are uncommon.

**Educational objective:**

Lacunar infarcts are small, ischemic infarcts (usually <15 mm) involving the deep brain structures (eg, basal ganglia, pons) and subcortical white matter (eg, internal capsule, corona radiata). They most often occur due to hypertension, which causes hardening/thickening of the vessel wall (hypertensive arteriolar sclerosis), predisposing patients with this condition to thrombotic vessel occlusion.

**References**

- Lacunar infarction and small vessel disease: pathology and pathophysiology.



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A 40-year-old woman is evaluated for neck pain that has gradually worsened over the past several months. The patient reports a pulling sensation in her neck that causes difficulty in keeping her head straight. She has had no trauma and has no other medical conditions. Physical examination shows a spastic and thickened sternocleidomastoid muscle causing head tilt. The patient is diagnosed with idiopathic torticollis. She is treated with injections of a bacterial product into the affected muscle, with significant relief of her symptoms. The substance administered to this patient is derived from bacteria that most likely demonstrate which of the following characteristics?

A. Antigenically hypervariable pili
B. Antiphagocytic capsule
C. IgG-binding outer membrane protein
D. Intracellular polyphosphate granules
E. Subterminal spore formation
F. Type III secretion system


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- A. Antigenically hypervariable pili (1%)
- B. Antiphagocytic capsule (4%)
- C. IgG-binding outer membrane protein (4%)
- D. Intracellular polyphosphate granules (4%)
- ✓ E. Subterminal spore formation (80%)
- F. Type III secretion system (5%)

Correct

80%

27 secs

11/01/2020



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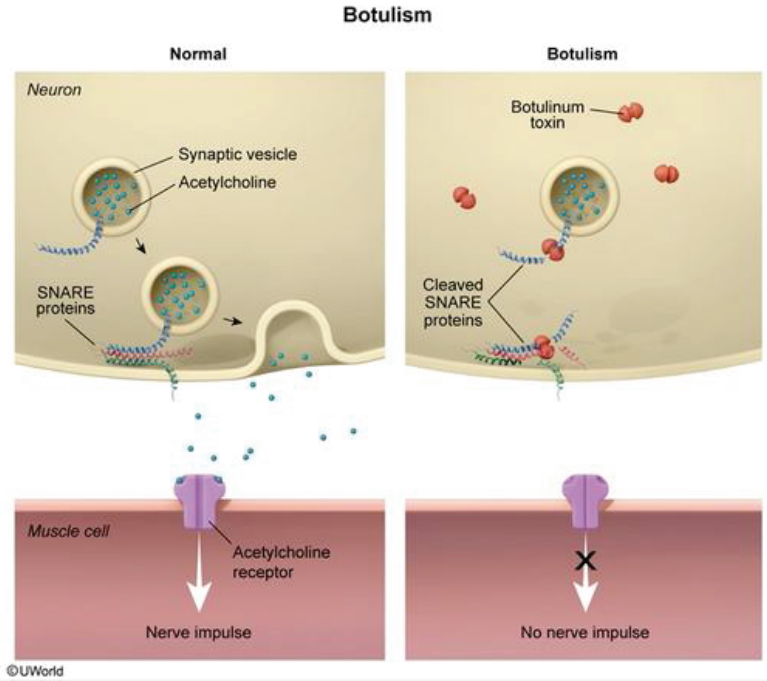


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*Clostridium botulinum* is a gram-positive, anaerobic bacillus that synthesizes botulinum toxin intracellularly and releases it by autolysis. **Botulinum toxin** prevents the presynaptic release of acetylcholine from the nerve terminal at the neuromuscular junction. This prevents both nicotinic and muscarinic activation, leading to **skeletal muscle weakness** and reduced glandular secretions, respectively. Botulism is a result of toxin ingestion and is characterized by cranial nerve deficits and descending symmetric paralysis. **Spore formation**, which occurs in the **subterminal location** (between the terminal end and center of the bacteria), allows the bacteria to survive adverse conditions (eg, heat, high-oxygen environment).

Focal dystonia is a localized, uncontrollable muscle contraction that can lead to pain and physical deformity. **Torticollis** is a common manifestation of dystonia and is due to involvement of the sternocleidomastoid muscle. Injection of botulinum toxin type B into the dystonic muscle results in muscular relaxation and **relief of symptoms**. Botulinum toxin can also be used to treat the muscle spasms of multiple sclerosis and Parkinson disease, to relax the lower esophageal sphincter in achalasia, and to reduce the appearance of facial wrinkles. The localized anticholinergic effect also makes it useful in the treatment of hyperhydrosis. The effects are temporary (approximately 3 months), due to the regeneration of the nerve terminal with time.

**(Choice A)** Hypervariable pili are characteristic of *Neisseria meningitidis* and *Neisseria gonorrhoeae*;


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regeneration of the nerve terminal with time.

**(Choice A)** Hypervariable pili are characteristic of *Neisseria meningitidis* and *Neisseria gonorrhoeae*; antigenic heterogeneity aids in immune evasion and allows for repeat infections.

**(Choice B)** The antiphagocytic capsule is a primary virulence factor for *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Klebsiella pneumonia*, and *Neisseria meningitidis*.

**(Choice C)** *Staphylococcus aureus* has an IgG-binding outer membrane protein—the protein A virulence factor—which binds the Fc portions of IgG, thereby preventing opsonization, phagocytosis, and complement fixation.

**(Choice D)** Intracellular polyphosphate granules are seen on methylene blue staining and are an identifying characteristic of *Corynebacterium diphtheriae*.

**(Choice F)** Type III secretion systems allow bacteria to inject proteins directly into host cells to avoid invoking an immune response. They are seen in many gram-negative bacteria, including *Shigella*, *Salmonella*, *Pseudomonas*, *Yersinia*, and enteropathogenic *Escherichia coli*.

**Educational objective:**

*Clostridium botulinum* is a spore-forming, gram-positive, anaerobic bacillus that synthesizes botulinum


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**(Choice C)** *Staphylococcus aureus* has an IgG-binding outer membrane protein—the protein A virulence factor—which binds the Fc portions of IgG, thereby preventing opsonization, phagocytosis, and complement fixation.

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**(Choice F)** Type III secretion systems allow bacteria to inject proteins directly into host cells to avoid invoking an immune response. They are seen in many gram-negative bacteria, including *Shigella*, *Salmonella*, *Pseudomonas*, *Yersinia*, and enteropathogenic *Escherichia coli*.

**Educational objective:**
*Clostridium botulinum* is a spore-forming, gram-positive, anaerobic bacillus that synthesizes botulinum toxin, which prevents the presynaptic release of acetylcholine from the nerve terminal at the neuromuscular junction. Botulinum toxin can be used to treat focal dystonia and other disorders of abnormal muscle contraction.

| Microbiology | Nervous System | Botulism |
|---|---|---|
| Subject | System | Topic |

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A 75-year-old man is brought to the emergency department after a syncopal episode at his assisted living facility. The event occurred an hour ago, when he was eating lunch with other residents of the facility. The patient suddenly slumped over onto the table and awakened spontaneously after about 30 seconds. He appeared pale afterwards but was not confused, and fingerstick blood glucose was normal. Medical history includes hypertension, type 2 diabetes mellitus, benign prostatic hyperplasia, and Alzheimer disease. Temperature is 37 C (98.6 F), supine and standing blood pressure is 110/68 mm Hg, and pulse is 62/min. The oropharyngeal mucosa is moist and jugular venous pressure is normal. The lungs are clear on auscultation and heart sounds are normal. The patient is hospitalized for observation and is found to have an episodic bradyarrhythmia and atrioventricular block. If this patient's condition is due to a medication, which of the following is the most likely cause?

A. Canagliflozin
B. Diphenhydramine
C. Donepezil
D. Lisinopril
E. Terazosin


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A. Canagliflozin
B. Diphenhydramine
C. Donepezil
D. Lisinopril
E. Terazosin

Submit



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A. Canagliflozin (5%)
B. Diphenhydramine (18%)
C. Donepezil (44%)
D. Lisinopril (8%)
E. Terazosin (23%)

Correct
44%
01 min, 26 secs
03/08/2021


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This patient's brief loss of consciousness is consistent with **syncope**, which occurs due to a **transient loss of cerebral perfusion**. Most episodes of syncope are benign, resulting from a vasovagal reflex that is triggered by emotional stress or prolonged standing. However, syncope may be a warning sign of a serious underlying pathology (eg, cardiac arrhythmia, severe aortic stenosis, pulmonary embolism). In addition, numerous **medications** can cause or contribute to syncope and should be considered.

**Acetylcholinesterase inhibitors** (eg, donepezil, rivastigmine) are commonly used in the management of Alzheimer dementia. Alzheimer dementia involves dysfunction of cholinergic pathways in the brain; therefore, inhibition of acetylcholinesterase and a consequent reduction in acetylcholine breakdown may improve cognitive function in some patients. However, this mechanism also produces **enhanced parasympathetic tone** that can lead to adverse effects. Underlying age-related degeneration of the conduction system is common in the elderly, and the effects of acetylcholinesterase inhibition can precipitate **bradycardia** and **atrioventricular block** in such patients. These conduction abnormalities lead to **reduced cardiac output** that may manifest as presyncope (ie, lightheadedness) or syncope.

**(Choices A, B, D and E)** Antihypertensive agents (eg, lisinopril) may contribute to orthostatic syncope (syncope that occurs with standing). By inhibiting vasoconstriction, these agents both prevent mobilization of venous blood that is pooled in the legs and impair the increase in arteriolar resistance needed to


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**Exhibit Display**

**Medication-induced orthostasis**

| Mechanism | Examples |
|---|---|
| α-1 blockade–mediated vasodilation | • Terazosin, prazosin, doxazosin<br>• Antipsychotics (eg, risperidone)<br>• Antihistamines, TCAs |
| Other vasodilation | • ACE inhibitors & ARBs<br>• Dihydropyridine CCBs<br>• Hydralazine, nitrates<br>• Phosphodiesterase inhibitors |
| Volume depletion | • Diuretics<br>• SGLT-2 inhibitors |
| Sympathetic blockade | • Beta blockers<br>• Clonidine |

**ARBs** = angiotensin receptor blockers; **CCBs** = calcium channel blockers; **SGLT** = sodium-glucose cotransporter; **TCAs** = tricyclic antidepressants.

New | Existing



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to **reduced cardiac output** that may manifest as presyncope (ie, lightheadedness) or syncope.

**(Choices A, B, D and E)** Antihypertensive agents (eg, lisinopril) may contribute to orthostatic syncope (syncope that occurs with standing). By inhibiting vasoconstriction, these agents both prevent mobilization of venous blood that is pooled in the legs and impair the increase in arteriolar resistance needed to maintain cerebral perfusion on standing. Terazosin (used for the treatment of benign prostatic hyperplasia) and first-generation histamine-1 blockers (eg, diphenhydramine) have alpha-1 receptor-blocking properties and may also contribute to orthostatic syncope via inhibited vasoconstriction. Sodium-glucose cotransporter-2 inhibitors (eg, canagliflozin) may contribute to orthostatic syncope by stimulating an osmotic diuresis that leads to hypovolemia. None of these agents cause syncope via the slowing of cardiac conduction and they would not explain this patient's episodic bradycardia and atrioventricular block.

**Educational objective:**
Syncope results from a transient loss of cerebral perfusion, and numerous medications can cause or contribute to syncope. Acetylcholinesterase inhibitors (eg, donepezil, rivastigmine) may cause syncope due to enhanced parasympathetic tone that leads to bradycardia and atrioventricular block with reduced cardiac output.


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A 61-year-old man comes to the office due to a painful rash on his face for the past 3 days. The patient has no other medical conditions and takes no medications. He is a retired schoolteacher and lives with his wife. Skin examination findings are shown in the exhibit. The remainder of the physical examination shows no abnormalities. Which of the following events most likely immediately preceded the appearance of skin rash in this patient?

A. Alteration in the patient's normal skin flora
B. Close physical contact with an infected person
C. Inhalation of pathogen-containing aerosols
D. Reactivation of latent organism in sensory ganglia
E. Waning of organism-specific antibodies

Submit



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A 61-year-old man comes to the office due to a painful rash on his face for the past 3 days. The patient has no other medical conditions and takes no medications. He is a retired schoolteacher and lives with his wife. Skin examination findings are shown in the exhibit. The remainder of the physical examination shows no abnormalities. Which of the following events most likely immediately preceded the appearance of skin rash in this patient?

A. Alteration in the patient's normal skin flora (3%)
B. Close physical contact with an infected person (3%)
C. Inhalation of pathogen-containing aerosols (8%)
✓ D. Reactivation of latent organism in sensory ganglia (82%)
E. Waning of organism-specific antibodies (1%)

Correct

82% Answered correctly

26 secs Time Spent

09/20/2020 Last Updated



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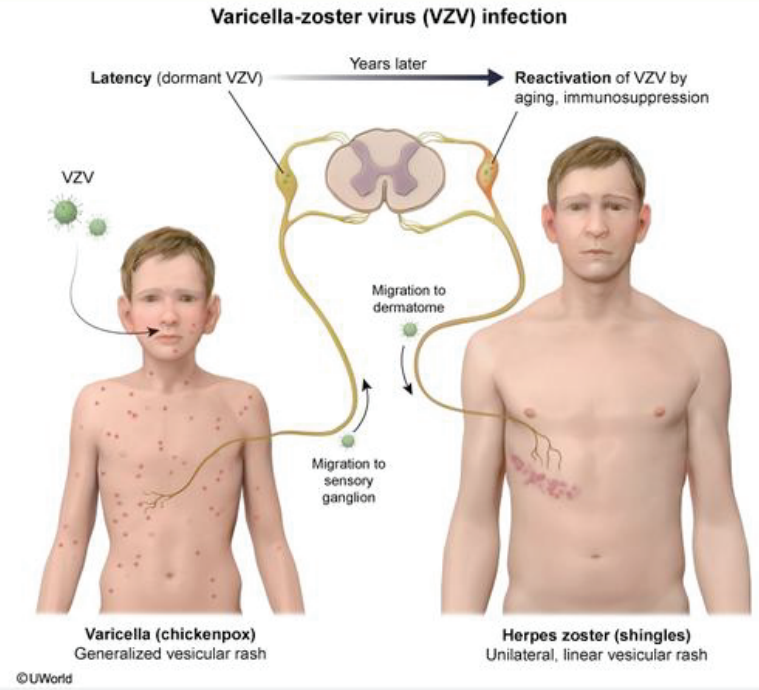


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This patient has a crusted vesicular rash in a dermatomal distribution consistent with **shingles** (herpes zoster). Shingles is caused by **reactivation** of **varicella-zoster virus** (VZV), a double-stranded DNA virus of the herpesvirus family. Primary VZV infection occurs most commonly in childhood. Inoculation in the nasopharyngeal mucosa is followed by migration of the virus to the regional lymphatics. Subsequent dermatotrophic migration produces a diffuse vesicular rash associated with fever, malaise, and pharyngitis (**chickenpox**). Then, the virus migrates via sensory nerves to **cranial nerve and dorsal spinal ganglia**, where it lies dormant for decades.

Most patients who have had primary chickenpox do not develop recurrent diffuse disease. Over time, however, waning cell-mediated immune function allows reactivation of the virus, which typically spreads down a single spinal nerve to cause a painful, erythematous, vesicular rash in a dermatomal distribution. The primary risk factor for reactivation is increasing age; other factors can include malignancy, autoimmune disease, and immune-suppressing therapy.

The varicella vaccine is recommended for prevention of primary disease in children, women of childbearing age, adults with sustained risk of exposure, and household contacts of immunocompromised hosts. Zoster vaccine is recommended for adults age ≥50 and reduces the risk of reactivation.



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**(Choice A)** Colonization of the skin by transient flora (eg, *Staphylococcus aureus*, *Candida* species, gram-negative bacilli) occasionally leads to clinical disease, especially following antibiotic exposure (eg, vaginal candidiasis). However, VZV does not remain on the surface of the skin for prolonged periods.

**(Choices B and C)** Primary VZV infection (ie, chickenpox) can be acquired by direct contact or airborne aerosol from patients with active chickenpox or zoster lesions. However, primary VZV infection causes diffuse lesions; lesions in a dermatomal distribution are seen only with reactivation from sensory ganglia.

**(Choice E)** Declining VZV-specific immunity increases the risk of reactivation. However, the immune response to VZV is primarily based on cell-mediated, rather than humoral (ie, antibodies), factors.

**Educational objective:**

Primary varicella-zoster virus infection (chickenpox) occurs most commonly in childhood. Subsequently, the virus migrates to the sensory ganglia, where it lies dormant for decades. Over time, waning cell-mediated immunity allows reactivation of the virus, which spreads down a single nerve to cause a painful, erythematous, vesicular rash in a dermatomal distribution.

**References**

- Molecular mechanisms of varicella zoster virus pathogenesis.



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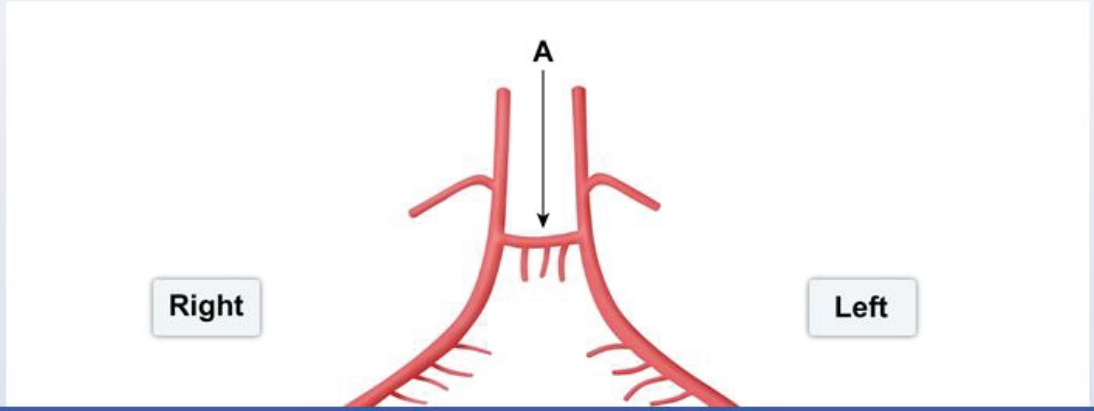
A 55-year-old, right-handed man comes to the emergency department due to recent onset of severe, throbbing, right-sided headache and double vision. His medical history includes poorly controlled hypertension and chronic tobacco use. Neurologic examination shows that he is awake, alert, and oriented and can follow commands. Visual fields and optic fundi are normal. The position of the right eye is down and out with ipsilateral ptosis, and the right pupil is dilated and nonreactive to both light and accommodation. Left eye examination is normal. Based on this patient's neurologic deficits, CT angiography of the head is most likely to reveal an aneurysm arising from which of the following locations in the image below?



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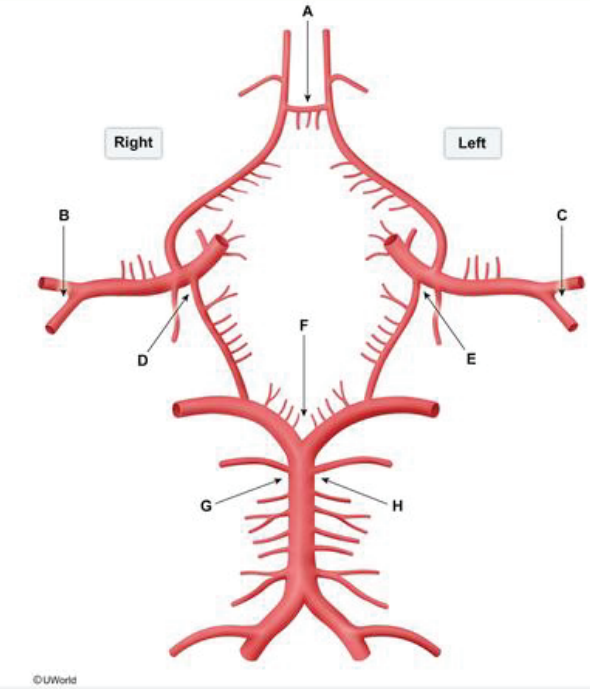


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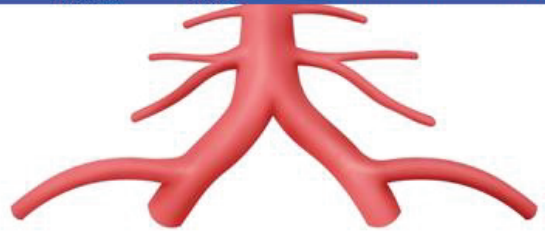

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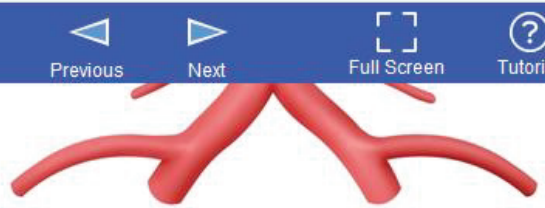

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- A. A (10%)
- B. B (6%)
- C. C (2%)
- ✓ D. D (45%)
- E. E (10%)
- F. F (6%)
- G. G (14%)
- H. H (4%)

45%
01 min, 53 secs
11/22/2020



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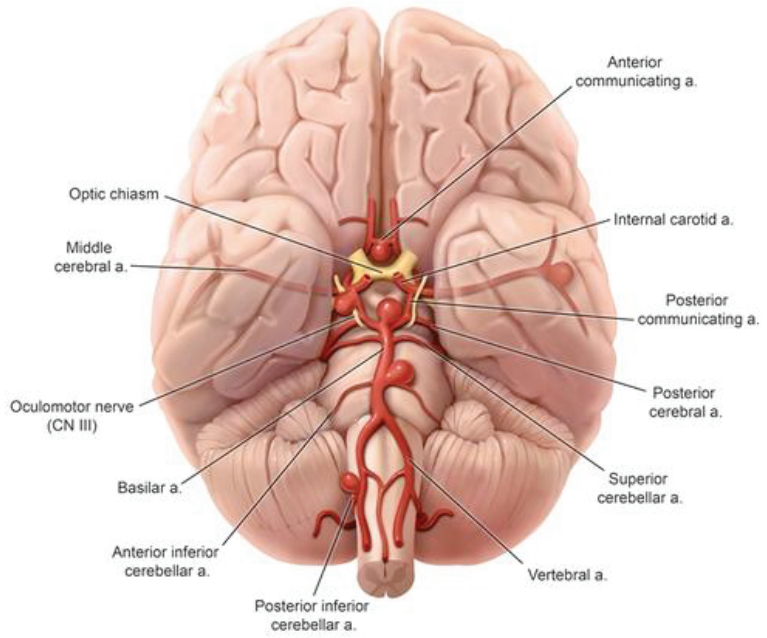
Berry (saccular) aneurysms

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This patient has right **oculomotor nerve (CN III) palsy** secondary to a compressive **aneurysm** arising from the junction of the right **posterior communicating artery** with the internal carotid artery. Saccular aneurysms typically arise from branch points on the circle of Willis, and most (85%) affect the anterior circulation (eg, anterior communicating, posterior communicating, and middle cerebral arteries). Chronic smoking and poorly controlled hypertension are risk factors. Unruptured aneurysms are usually asymptomatic, but patients may experience headache and cranial neuropathies due to mass effect.

CN III is a pure motor nerve that exits the midbrain between the posterior cerebral and superior cerebellar arteries and courses along the posterior communicating artery, making it particularly susceptible to injury from posterior communicating artery aneurysms. It carries general visceral efferent fibers on its surface (for the pupillary light and near-reflex pathways) and general somatic efferent fibers within its interior (innervating superior rectus, inferior rectus, medial rectus, inferior oblique, and levator palpebrae superioris muscles). Consequently, aneurysmal compression of CN III produces **mydriasis** (due to superficial parasympathetic fiber damage) with diplopia, **ptosis**, and **down and out deviation** of the ipsilateral eye (due to somatic efferent fiber injury).

**(Choice A)** The junction of the anterior communicating artery and anterior cerebral artery is the most common location for saccular aneurysms; however, aneurysms in this region typically compress the central



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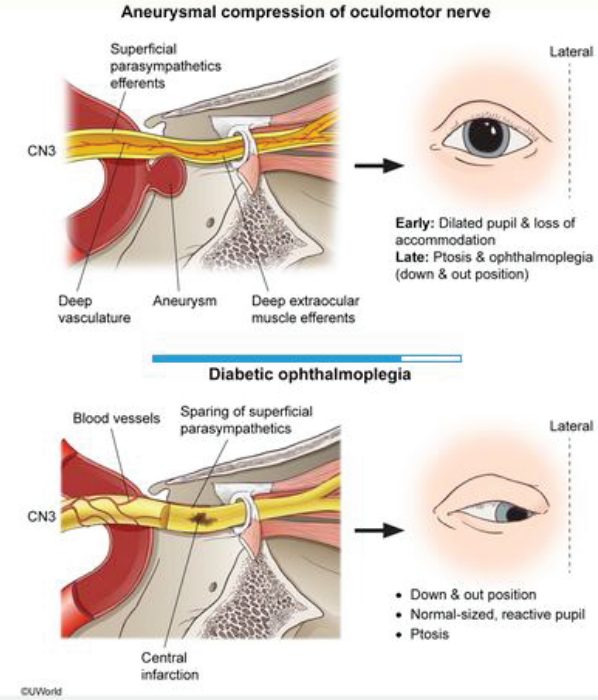


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common location for saccular aneurysms; however, aneurysms in this region typically compress the central optic chiasm, causing bitemporal hemianopia.

**(Choices B and C)** Saccular aneurysms of the middle cerebral artery typically occur at its distal bifurcation and do not usually affect the oculomotor nerve.

**(Choice E)** Posterior communicating artery aneurysms cause symptoms on the same side as the lesion due to damage to the ipsilateral oculomotor nerve. A left posterior communicating artery aneurysm would cause left-sided mydriasis, ptosis, and eye deviation.

**(Choices F, G, and H)** Approximately 15% of saccular aneurysms arise from the posterior circulation (eg, branches of the basilar and vertebral arteries). Although these aneurysms could potentially cause oculomotor palsy by compressing the oculomotor nerve as it exits the midbrain, this presentation is rare and usually associated only with very large aneurysms that cause multiple neurologic deficits.

**Educational objective:**
The oculomotor nerve (CN III) is most susceptible to injury from ipsilateral posterior communicating artery aneurysms. Aneurysmal compression of CN III produces mydriasis (due to superficial parasympathetic fiber damage) with diplopia, ptosis, and down and out deviation of the ipsilateral eye (due to somatic efferent fiber injury).


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A 38-year-old woman comes to the emergency department due to 2 days of headache, nausea, and photophobia. She has had migraines since her early 20s but has had more frequent episodes over the last few years. The current headache is more severe than usual, and ibuprofen did not relieve the pain. A flulike illness preceded the symptoms. Temperature is 38.3 C (100.9 F), blood pressure is 144/86 mm Hg, and pulse is 110/min. The patient appears lethargic. Cranial nerves, sensation, and motor functions are normal. She reports neck pain when instructed to touch the chest with her chin. No skin rash is present. Noncontrast CT scan of the head shows no abnormalities. Which of the following is the best next step in management of this patient?

A. 100% oxygen inhalation
B. Lumbar puncture
C. Metoclopramide
D. MRI of the brain
E. Sumatriptan
F. Topiramate


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few years. The current headache is more severe than usual, and ibuprofen did not relieve the pain. A flulike illness preceded the symptoms. Temperature is 38.3 C (100.9 F), blood pressure is 144/86 mm Hg, and pulse is 110/min. The patient appears lethargic. Cranial nerves, sensation, and motor functions are normal. She reports neck pain when instructed to touch the chest with her chin. No skin rash is present. Noncontrast CT scan of the head shows no abnormalities. Which of the following is the best next step in management of this patient?

A. 100% oxygen inhalation (1%)
B. Lumbar puncture (84%)
C. Metoclopramide (0%)
D. MRI of the brain (4%)
E. Sumatriptan (7%)
F. Topiramate (0%)

Correct

84%

54 secs

01/30/2021



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Although migraine headaches are often associated with photophobia and nausea, this patient's fever, stiff neck, and lethargy make **bacterial meningitis** the far more likely diagnosis. Bacterial meningitis is most commonly caused by *Streptococcus pneumoniae* and *Neisseria meningitidis*. These pathogens colonize the host's mucous membranes, spread into the bloodstream, and penetrate the blood-brain barrier. A lack of humoral components (eg, complement system, immunoglobulins) within the central nervous system allows bacteria to rapidly proliferate within the cerebrospinal fluid. The resultant cytokine-mediated inflammatory response causes the classic **triad** of symptoms: **high fever** (>38 C [100.4 F]), **stiff neck**, and **altered level of consciousness**. A generalized severe headache is also usually present.

Patients with suspected bacterial meningitis require urgent blood cultures, empiric antibiotics, and **lumbar puncture** with cerebrospinal fluid analysis to confirm the diagnosis, identify the underlying pathogen, and determine antibiotic sensitivity.

**(Choice A)** 100% oxygen can be used to abort cluster headaches, which are seen primarily in men and are usually characterized by severe orbital or periorbital pain, restless agitation, and autonomic symptoms (eg, lacrimation, rhinorrhea, ptosis, miosis). Fever and nuchal rigidity would be atypical.

**(Choices C, E, and F)** Metoclopramide and sumatriptan can be used to abort acute migraines; topiramate is an effective treatment for the prevention of chronic migraine headaches. Migraines are usually


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(eg, lacrimation, rhinorrhea, ptosis, miosis). Fever and nuchal rigidity would be atypical.

**(Choices C, E, and F)** Metoclopramide and sumatriptan can be used to abort acute migraines; topiramate is an effective treatment for the prevention of chronic migraine headaches. Migraines are usually characterized by a unilateral throbbing headache with or without associated symptoms such as nausea, aura, or photophobia. Fever, nuchal rigidity, and lethargy would be atypical.

**(Choice D)** MRI of the brain can be used to evaluate for potential brain tumor. Patients with brain tumors commonly develop dull, constant headaches, focal neurologic symptoms, and seizures. Fever would be atypical. Although brain imaging is often recommended prior to lumbar puncture to evaluate for signs of elevated intracranial pressure, non-contrast head CT is used primarily because it offers rapid results and fewer treatment delays. This patient had a negative head CT; MRI would not be necessary prior to LP.

**Educational objective:**

The classic triad of fever, stiff neck, and altered mentation should raise suspicion for acute bacterial meningitis. Evaluation requires prompt blood cultures, empiric antibiotics, and lumbar puncture with cerebrospinal fluid analysis.

**References**

- The evaluation and management of bacterial meningitis: current practice and emerging developments.



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www.ncbi.nlm.nih.gov/pubmed/20445424

A 74-year-old woman comes to the office due to progressive forgetfulness over the past 2 years. Her family states that the patient asks the same questions repeatedly over the course of a day and often forgets what she is doing in the middle of chores. The patient has also been more irritable but has had no movement or gait abnormalities, feelings of depression, hallucinations, or delusions. Medical conditions include hypertension and renal artery stenosis. Vital signs are within normal limits. Mini-Mental State Examination score is 21 out of 30 and she recalls 1 out of 3 objects after 5 minutes. There are no focal neurologic deficits. Which of the following is most likely involved in the pathogenesis of this patient's condition?

A. Alpha-synuclein protein aggregation
B. $CD4^+$ T lymphocytes activated by myelin basic protein
C. Inflammatory vasculitis affecting the arterioles
D. Microtubule-associated protein polymerization
E. Perivascular infiltration of virally infected macrophages


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family states that the patient asks the same questions repeatedly over the course of a day and often forgets what she is doing in the middle of chores. The patient has also been more irritable but has had no movement or gait abnormalities, feelings of depression, hallucinations, or delusions. Medical conditions include hypertension and renal artery stenosis. Vital signs are within normal limits. Mini-Mental State Examination score is 21 out of 30 and she recalls 1 out of 3 objects after 5 minutes. There are no focal neurologic deficits. Which of the following is most likely involved in the pathogenesis of this patient's condition?

A. Alpha-synuclein protein aggregation (39%)

B. ~~CD4+ T lymphocytes activated by myelin basic protein~~ (1%)

C. Inflammatory vasculitis affecting the arterioles (8%)

D. Microtubule-associated protein polymerization (49%)

E. ~~Perivascular infiltration of virally infected macrophages~~ (0%)

Incorrect
Correct answer

49%

02 mins, 06 secs

02/05/2021



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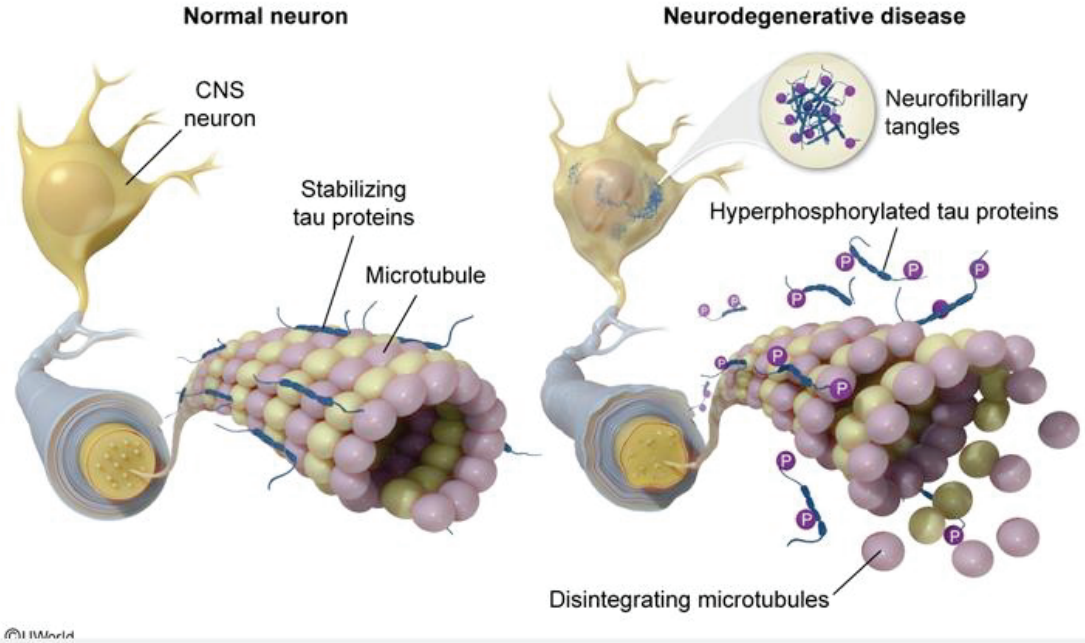
## Tau protein in neurodegenerative disease

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This older patient with impairment of recent memory and cognitive deficits in the absence of other focal neurologic findings most likely has **Alzheimer disease** (AD). Neuropathologic features of AD include:

- **Neurodegeneration**, leading to neuronal loss (microscopic) and cerebral atrophy (macroscopic)
- **Beta-amyloid plaques**: excess beta amyloid forms insoluble fibrils that accumulate into extracellular amyloid plaques
- **Neurofibrillary tangles**: aggregates of hyperphosphorylated tau protein form intracellular tangled clumps

**Tau** is a protein associated with **neuronal microtubules**. Under normal conditions, tau takes part in microtubule stabilization. In AD, tau is **hyperphosphorylated** and disassociates from the microtubules, which may lead to instability and disrupted axonal transport. Hyperphosphorylated tau also makes **paired helical filaments**, which create **intracellular neurofibrillary tangles**, resulting in neuronal damage. Increased accumulation of these tangles is associated with progression of AD.

**(Choice A)** Dementia with Lewy bodies (ie, alpha-synuclein protein aggregation) is characterized by fluctuating cognitive impairment, dysautonomia, parkinsonism, and visual hallucinations. This patient's progressive impairment of recent memory and unremarkable neurologic examination are more consistent



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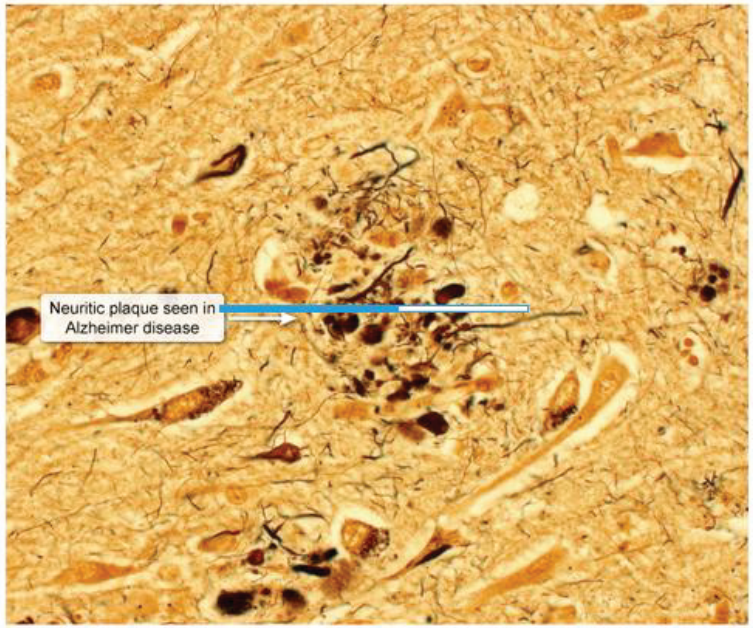
**Alzheimer disease**

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progressive impairment of recent memory and unremarkable neurologic examination are more consistent



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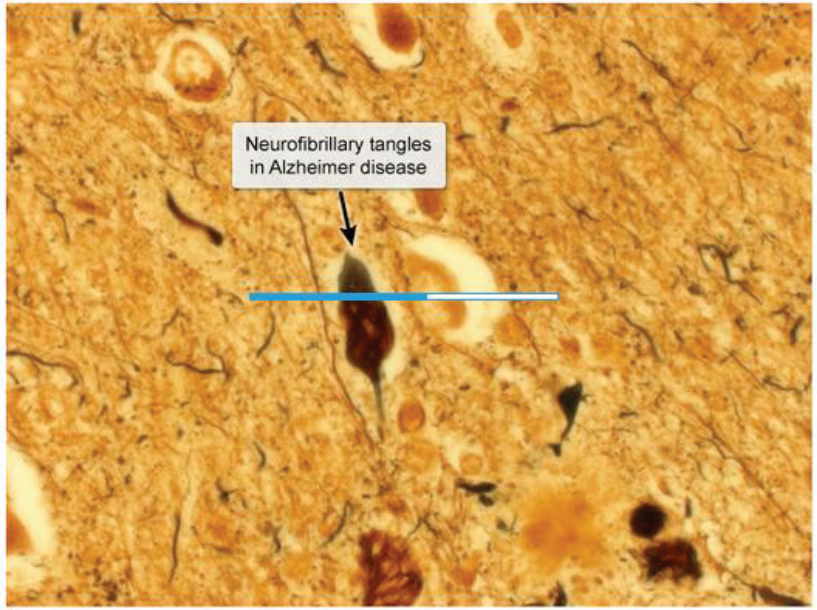
Alzheimer disease

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progressive impairment of recent memory and unremarkable neurologic examination are more consistent



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**(Choice A)** Dementia with Lewy bodies (ie, alpha-synuclein protein aggregation) is characterized by fluctuating cognitive impairment, dysautonomia, parkinsonism, and visual hallucinations. This patient's progressive impairment of recent memory and unremarkable neurologic examination are more consistent with AD.

**(Choice B)** Multiple sclerosis (MS) is an autoimmune disease targeting oligodendrocytes, the myelin-producing cells of the CNS. The pathogenesis involves inappropriate activation of $CD4^+$ T lymphocytes by myelin basic protein. MS typically presents in young women (age <50) with neurologic deficits (eg, blurry vision, diplopia, focal weakness/numbness, bowel/bladder dysfunction) disseminated in time and space.

**(Choice C)** This older patient with hypertension and renal artery stenosis likely has significant atherosclerosis; however, there is no evidence of vasculitis. Vasculitis affecting the CNS often presents with headache and focal neurologic deficits, rather than progressive memory impairment, due to obstruction of the inflamed vessels and subsequent tissue ischemia.

**(Choice E)** Perivascular macrophage infiltration is characteristic of HIV-associated dementia, which occurs almost exclusively in untreated HIV-infected patients with advanced disease (eg, $CD4^+$ <200). In contrast to the cortical dysfunction (ie, amnestic symptoms) seen in AD, HIV-associated dementia is a subcortical dementia characterized by apathy, early attention impairment, and subcortical motor symptoms.


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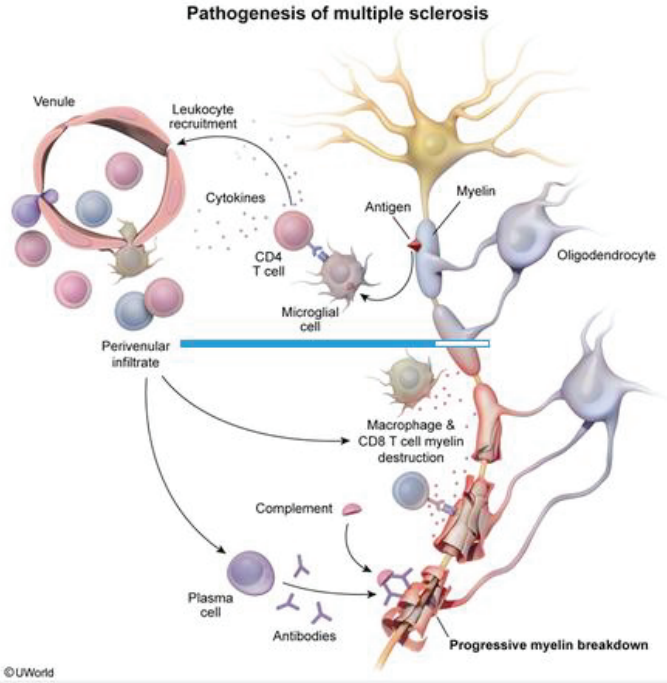


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atherosclerosis; however, there is no evidence of vasculitis. Vasculitis affecting the CNS often presents with headache and focal neurologic deficits, rather than progressive memory impairment, due to obstruction of the inflamed vessels and subsequent tissue ischemia.

**(Choice E)** Perivascular macrophage infiltration is characteristic of HIV-associated dementia, which occurs almost exclusively in untreated HIV-infected patients with advanced disease (eg, $CD4^+$ <200). In contrast to the cortical dysfunction (ie, amnestic symptoms) seen in AD, HIV-associated dementia is a subcortical dementia characterized by apathy, early attention impairment, and subcortical motor symptoms.

**Educational objective:**
Neuropathologic features of Alzheimer disease include neurodegeneration, amyloid plaques (ie, extracellular accumulations of beta amyloid), and neurofibrillary tangles. Neurofibrillary tangles are formed when tau, a protein associated with neuronal microtubules, becomes hyperphosphorylated and disassociates from the microtubules to form paired helical filaments.

| Pathophysiology | Nervous System | Alzheimer disease |
|---|---|---|
| Subject | System | Topic |

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A 62-year-old man comes to the office with his wife due to behavioral changes. The patient has become increasingly impulsive and irritable over the past 1-2 years. He recently lost his job after making inappropriate comments and touching female coworkers. The patient has also lost interest in his hobbies and appears withdrawn during social gatherings. His other medical problems are hypertension and hyperlipidemia. A thorough neuropsychological assessment is conducted. Inability to perform which of the following tasks would be most indicative of frontal lobe dysfunction?

A. Comprehending the meaning of a sentence
B. Describing similarities between a watch and a ruler
C. Differentiating between right and left
D. Identifying which finger is touched
E. Recognizing familiar faces

Submit



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A. Comprehending the meaning of a sentence (17%)
B. Describing similarities between a watch and a ruler (59%)
C. Differentiating between right and left (4%)
D. Identifying which finger is touched (2%)
E. Recognizing familiar faces (16%)

Correct

59%
Answered correctly

26 secs
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02/26/2021
Last Updated



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The **frontal lobes** are involved in a wide array of functions, including **personality**, **language**, **motor functions**, and **executive functions**. Executive functions include **abstraction**, planning, impulse inhibition, attention, and working memory. Abstraction may be tested by asking a patient to describe the similarities between two objects (eg, a watch and ruler both measure things). Patients with frontal lobe damage may be unable to provide an answer or may provide concrete answers such as "they both have numbers."

Because of its role in personality and impulse inhibition, processes that damage the frontal lobe (eg, traumatic brain injury, frontotemporal dementia) may lead to significant changes in behavior. Behavior change is more likely with bilateral, rather than unilateral, injury. Patients with frontal lobe injury may be disinhibited, socially inappropriate, irritable, and impulsive.

**(Choice A)** Impaired language comprehension (ie, Wernicke aphasia) results from lesions in the dominant superior temporal gyrus.

**(Choices C and D)** Patients with lesions in the dominant angular and supramarginal gyri (located in the parietal lobe) may have right-left disorientation and finger agnosia (ie, inability to recognize fingers). When these symptoms are accompanied by agraphia (ie, inability to write) and acalculia (ie, inability to perform arithmetic), it is known as Gerstmann syndrome.


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**(Choices C and D)** Patients with lesions in the dominant angular and supramarginal gyri (located in the parietal lobe) may have right-left disorientation and finger agnosia (ie, inability to recognize fingers). When these symptoms are accompanied by agraphia (ie, inability to write) and acalculia (ie, inability to perform arithmetic), it is known as Gerstmann syndrome.

**(Choice E)** The inability to recognize a familiar face (ie, prosopagnosia) may result from lesions in the fusiform gyrus (located in the temporal and occipital lobes).

**Educational objective:**

The frontal lobes are involved in personality, language, motor functions, and executive functions (eg, abstraction). Frontal lobe function may be diagnosed by testing abstraction ability (eg, asking about the similarities between two related objects) on the mental status examination.

**References**

- Why do patients with neurodegenerative frontal syndrome fail to answer: 'In what way are an orange and a banana alike?'

| Pathophysiology | Nervous System | Frontotemporal dementia |
|---|---|---|
| Subject | System | Topic |



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A 53-year-old man is evaluated for right hand discomfort. A month ago, he started to intermittently experience a "pins and needles" sensation in his right hand that is worse at night. He has no neck pain or history of trauma to the right upper extremity. The patient has smoked a pack of cigarettes daily for 20 years and has worked as an accountant for the past 30 years. On physical examination, there is loss of sensation over the right fifth digit. There is no swelling, redness, or warmth of the hand. The patient is most likely to have weakness of which of the following movements?

A. Elbow extension
B. Shoulder abduction
C. Wrist abduction
D. Wrist adduction
E. Wrist extension

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A 53-year-old man is evaluated for right hand discomfort. A month ago, he started to intermittently experience a "pins and needles" sensation in his right hand that is worse at night. He has no neck pain or history of trauma to the right upper extremity. The patient has smoked a pack of cigarettes daily for 20 years and has worked as an accountant for the past 30 years. On physical examination, there is loss of sensation over the right fifth digit. There is no swelling, redness, or warmth of the hand. The patient is most likely to have weakness of which of the following movements?

- A. ~~Elbow extension~~ (4%)
- B. ~~Shoulder abduction~~ (0%)
- C. Wrist abduction (16%)
- ✓ D. Wrist adduction (63%)
- E. ~~Wrist extension~~ (14%)

Correct

63% Answered correctly

01 min, 27 secs Time Spent

02/09/2021 Last Updated



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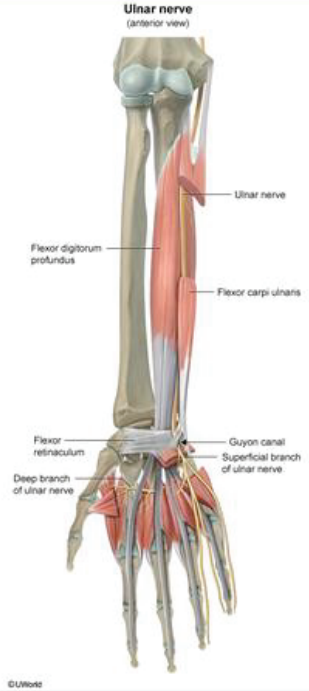


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profundus



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The **ulnar nerve** originates from the medial cord of the brachial plexus, courses with the brachial artery in the upper arm, and enters the forearm after passing posterior to the **medial epicondyle** of the humerus (cubital tunnel). It innervates flexor carpi ulnaris (wrist flexion and adduction) and the medial portion of flexor digitorum profundus before entering the wrist through Guyon canal (between the hook of the hamate and pisiform). In the hand, the superficial branch of the ulnar nerve provides cutaneous innervation to the **fifth digit**, medial half of the fourth digit, and the **hypothenar eminence**. The deep motor branch supplies most of the intrinsic muscles of the hand.

The ulnar nerve is most commonly injured at the elbow due to trauma (eg, medial epicondyle fracture) or **compression** (eg, resting on a hard surface while using a computer). Ulnar neuropathy at the elbow usually presents with discomfort and loss of sensation/paresthesia in the ulnar distribution. Severe cases can also result in **impaired wrist flexion and adduction** (ie, ulnar deviation) along with **finger weakness/clumsiness**. The nerve can also be injured more distally at the wrist as it runs through Guyon canal, resulting in more pronounced clawing of the 4th and 5th digits (ulnar claw) due to sparing of the flexor digitorum profundus.

**(Choices A and E)** Radial nerve injury (eg, C6/C7 disc herniation, humerus fracture) can result in weakness in elbow and/or wrist extension in addition to sensory loss over the posterior arm, dorsolateral



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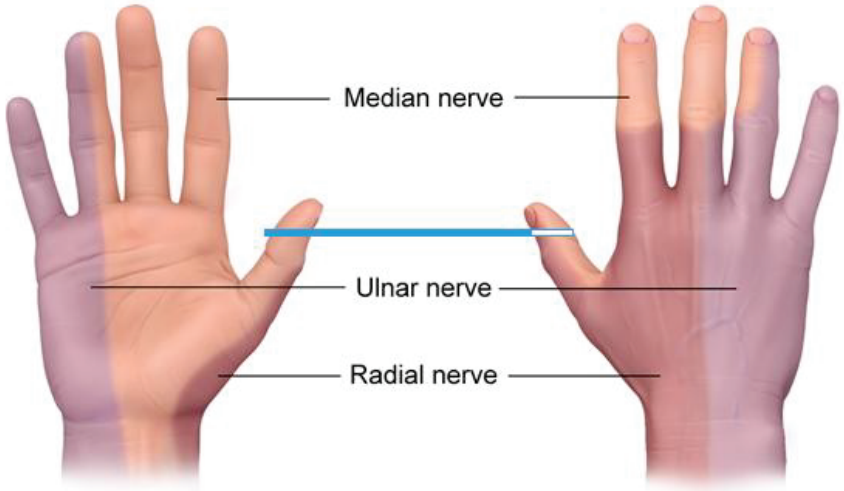
Cutaneous innervation of the hand

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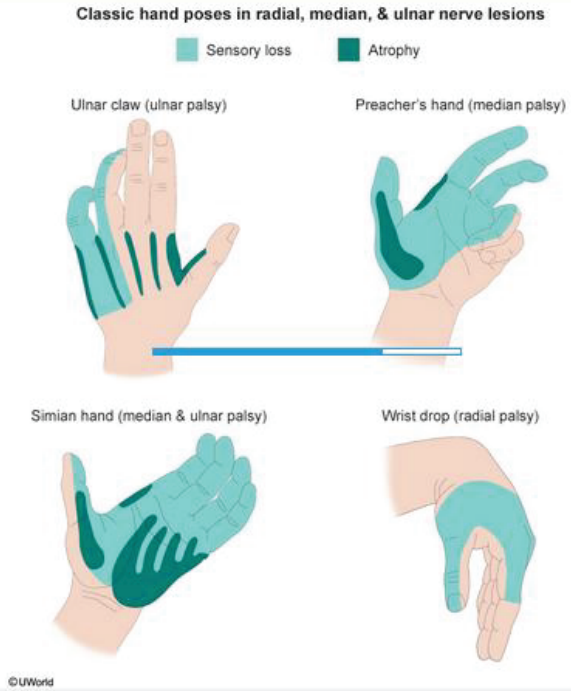


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flexor digitorum profundus.

**(Choices A and E)** Radial nerve injury (eg, C6/C7 disc herniation, humerus fracture) can result in weakness in elbow and/or wrist extension in addition to sensory loss over the posterior arm, dorsolateral hand, and dorsal thumb.

**(Choice B)** Axillary nerve injury (eg, shoulder dislocation, humeral fracture) can present with loss of sensation over the lateral upper arm and weakness in shoulder abduction (eg, deltoid weakness).

**(Choice C)** Proximal median nerve injury (eg, trauma) can result in weakness on wrist flexion and abduction (ie, radial deviation), flexion of the second/third digits, and flexion/opposition of the thumb along with palmar sensory loss involving the majority of the first through third digits.

**Educational objective:**

Ulnar nerve injury most commonly occurs at the elbow (eg, compression due to resting arm on a hard surface while using a computer) and usually presents with discomfort and sensory loss/paresthesia in the fifth digit, medial half of the fourth digit, and the hypothenar eminence. In severe cases, patients can also have weakness on wrist flexion and adduction (ie, ulnar deviation) along with finger weakness/clumsiness.

**References**

- Entrapment neuropathies I: upper limb (carpal tunnel excluded).



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A 14-year-old boy is brought to the physician by his mother for seizures. His seizures are usually characterized as a blank stare and lip smacking, followed by generalized shaking. The patient occasionally bites his tongue during the episodes and feels confused afterwards. His seizures have been refractory to various antiepileptic medications, and he is started on lamotrigine. The patient should be instructed to see his physician immediately if which of the following symptoms occurs?

- A. Abdominal pain
- B. Cough
- C. Diarrhea
- D. Heartburn
- E. Skin rash
- F. Urine discoloration

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A 14-year-old boy is brought to the physician by his mother for seizures. His seizures are usually characterized as a blank stare and lip smacking, followed by generalized shaking. The patient occasionally bites his tongue during the episodes and feels confused afterwards. His seizures have been refractory to various antiepileptic medications, and he is started on lamotrigine. The patient should be instructed to see his physician immediately if which of the following symptoms occurs?

- A. Abdominal pain (3%)
- B. Cough (0%)
- C. Diarrhea (0%)
- D. Heartburn (0%)
- ✓ E. Skin rash (86%)
- F. Urine discoloration (7%)

Correct

86% Answered correctly

30 secs Time Spent

03/11/2021 Last Updated



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A 14-year-old boy is brought to the physician by his mother for seizures. His seizures are usually characterized as a blank stare and lip smacking, followed by generalized shaking. The patient occasionally bites his tongue during the episodes and feels confused afterwards. His seizures have been refractory to various antiepileptic medications, and he is started on lamotrigine. The patient should be instructed to see his physician immediately if which of the following symptoms occurs?

- A. Abdominal pain (3%)
- B. Cough (0%)
- C. Diarrhea (0%)
- D. Heartburn (0%)
- ✓ E. Skin rash (86%)
- F. Urine discoloration (7%)

Correct

86% Answered correctly

30 secs Time Spent

03/11/2021 Last Updated



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**Lamotrigine** is an anticonvulsant that works by **blocking** voltage-gated **sodium channels**. It can be used to treat partial and generalized seizures and is also effective for bipolar disorder.

Up to 10% of patients using lamotrigine will develop benign rash; however, a potentially life-threatening rash due to **Stevens-Johnson syndrome** (SJS) or **toxic epidermal necrolysis** (TEN) occurs in up to 1% of patients (particularly children). SJS and TEN represent different endpoints along the same disease continuum: SJS involves <10% of the body surface area and TEN has >30% involvement. Patients with SJS/TEN typically develop flu-like symptoms (eg, fever, malaise, myalgias) followed by extensive cutaneous and mucosal lesions. Histopathologically, lesions are characterized by epidermal necrosis and subepidermal bullae.

The first appearance of rash requires discontinuation of the drug immediately as SJS/TEN and benign rash cannot be distinguished reliably. Other anticonvulsants associated with SJS/TEN include carbamazepine, phenobarbital, and phenytoin.

**(Choices A, C, and D)** Gastrointestinal symptoms (eg, abdominal pain, heartburn, diarrhea) are relatively common with lamotrigine and other anticonvulsant medications but are usually not life-threatening.

**(Choices B and F)** Although SJS/TEN can present with a flu-like prodrome (eg, fever, malaise, myalgia), cough or urinary symptoms would be atypical


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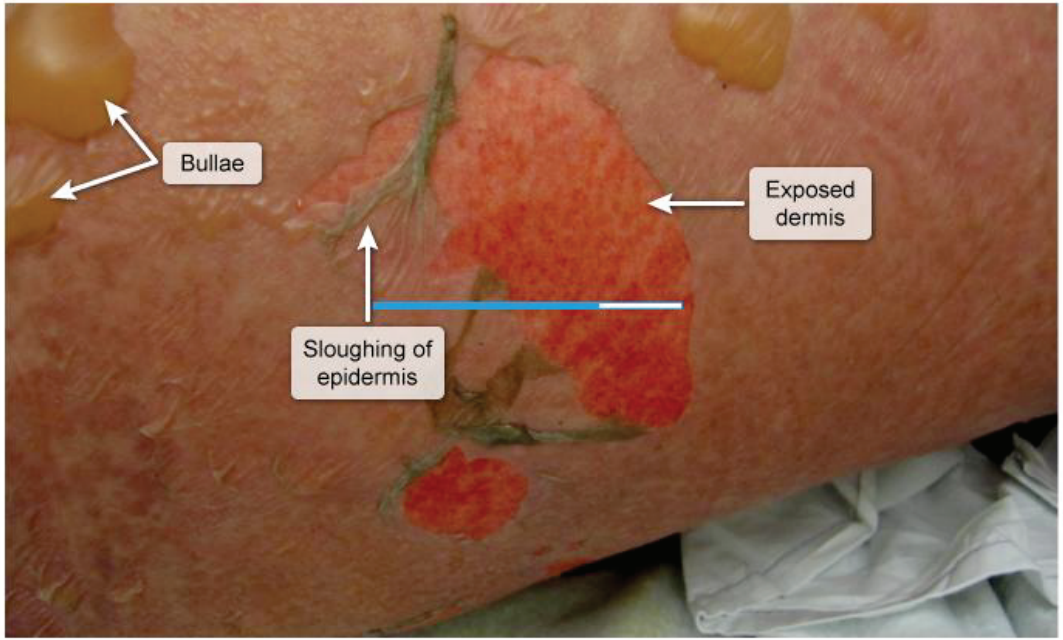
Exhibit Display

**Toxic epidermal necrolysis**

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cough or urinary symptoms would be atypical



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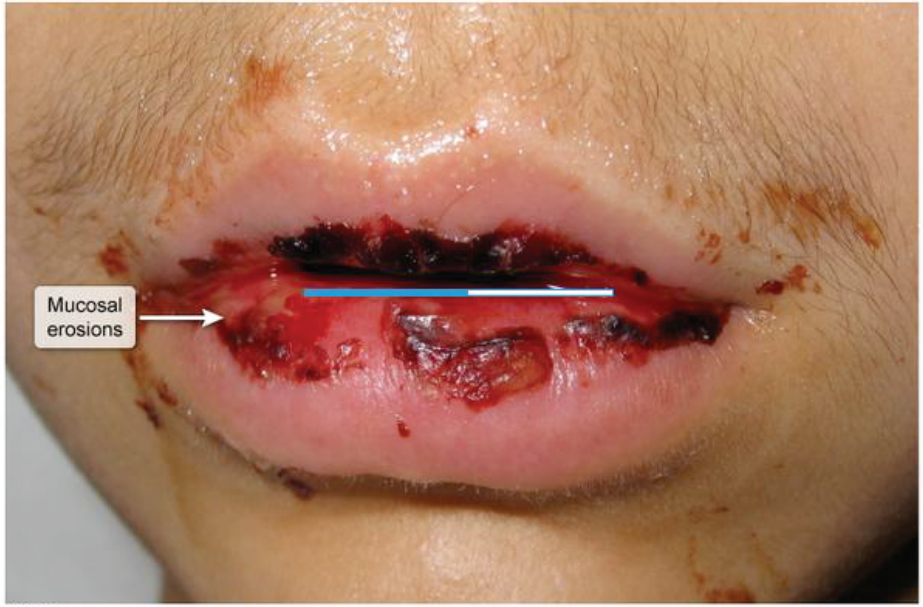
Exhibit Display

Stevens-Johnson syndrome

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cough or urinary symptoms would be atypical



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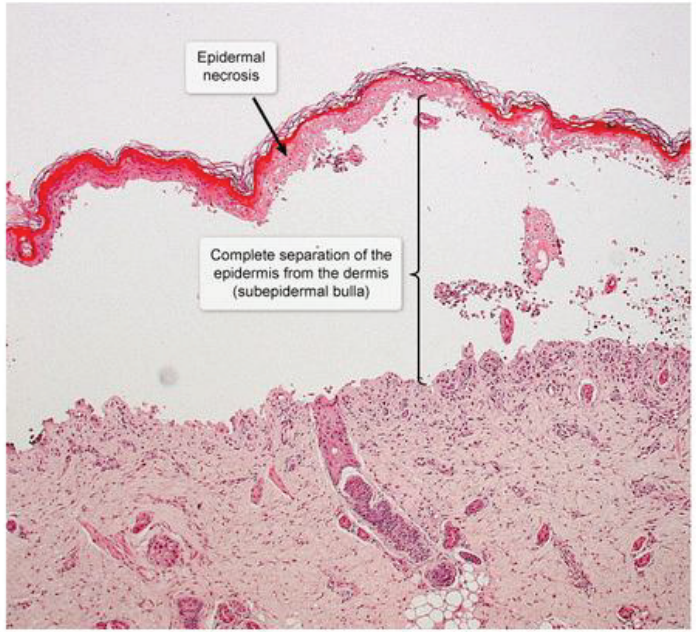
## Exhibit Display

**Toxic epidermal necrolysis**

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cough or urinary symptoms would be atypical



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The first appearance of rash requires discontinuation of the drug immediately as SJS/TEN and benign rash cannot be distinguished reliably. Other anticonvulsants associated with SJS/TEN include carbamazepine, phenobarbital, and phenytoin.

**(Choices A, C, and D)** Gastrointestinal symptoms (eg, abdominal pain, heartburn, diarrhea) are relatively common with lamotrigine and other anticonvulsant medications but are usually not life-threatening.

**(Choices B and F)** Although SJS/TEN can present with a flu-like prodrome (eg, fever, malaise, myalgia), cough or urinary symptoms would be atypical.

**Educational objective:**
Lamotrigine can be used to treat partial and generalized seizures and works by blocking voltage-gated sodium channels. Stevens-Johnson syndrome and toxic epidermal necrolysis are rare, life-threatening adverse effects characterized by flu-like symptoms followed by widespread mucocutaneous epidermal necrosis.

| Pharmacology | Nervous System | Antiepileptics |
|---|---|---|
| Subject | System | Topic |

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A 66-year-old man comes to the office with diplopia that progressively worsens toward the end of the day. The patient has no shortness of breath, trouble swallowing, or generalized weakness. He is currently receiving low-dose pyridostigmine for treatment of his condition and claims good compliance without significant side effects. Physical examination reveals fatigable asymmetric ptosis and binocular horizontal diplopia. Infusion of edrophonium elicits a significant improvement in his symptoms. Which of the following is the best next step in management of this patient?

A. Add atropine
B. Administer pralidoxime
C. Change long-term therapy to edrophonium
D. Increase pyridostigmine dosage
E. Stop pyridostigmine temporarily

Submit



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A 66-year-old man comes to the office with diplopia that progressively worsens toward the end of the day. The patient has no shortness of breath, trouble swallowing, or generalized weakness. He is currently receiving low-dose pyridostigmine for treatment of his condition and claims good compliance without significant side effects. Physical examination reveals fatigable asymmetric ptosis and binocular horizontal diplopia. Infusion of edrophonium elicits a significant improvement in his symptoms. Which of the following is the best next step in management of this patient?

A. Add atropine (2%)
B. Administer pralidoxime (4%)
C. Change long-term therapy to edrophonium (4%)
✓ D. Increase pyridostigmine dosage (78%)
E. Stop pyridostigmine temporarily (10%)

Correct

78%
Answered correctly

42 secs
Time Spent

09/22/2020
Last Updated



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**Myasthenia gravis** is an autoimmune disease caused by autoantibodies directed against nicotinic acetylcholine receptors on the postsynaptic membrane of the neuromuscular junction. Action potential propagation is impaired in these patients as antibody binding leads to receptor degradation and complement-mediated damage of the postsynaptic membrane. Patients typically present with fluctuating weakness that worsens over the course of the day and most often involves the extraocular (eg, ptosis, diplopia) and bulbar (eg, fatigable chewing, dysphagia) muscles.

Acetylcholinesterase (AChE) is an enzyme that degrades acetylcholine in the synaptic cleft. Long-acting **AChE inhibitors** (eg, **pyridostigmine**) are used in the symptomatic treatment of myasthenia gravis as they increase acetylcholine concentration in the neuromuscular junction, prolonging its effect on the postsynaptic membrane.

Exacerbations of myasthenia gravis in patients being treated with AChE inhibitors may occur for 2 reasons. First, if the patient is undertreated (receives suboptimal doses of medication), not enough acetylcholine is available in the neuromuscular junction (**myasthenic crisis**). Infusion of the short-acting AChE inhibitor edrophonium (**Tensilon test**) increases neuromuscular transmission and can provide temporary improvement in symptoms **(Choice C)**. The pyridostigmine dose should be increased in the long-term management of these patients.


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**Myasthenia gravis** is an autoimmune disease caused by autoantibodies directed against nicotinic

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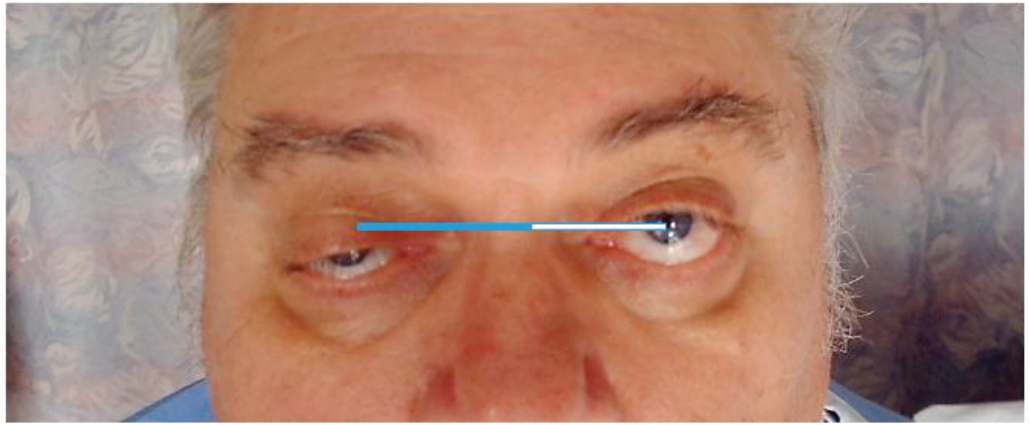

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The second (rare) cause of exacerbation is **cholinergic crisis**. In this condition, a patient receives inappropriately high doses of AChE inhibitor and has excessive acetylcholine in the synaptic cleft. This causes excessive stimulation of the skeletal muscles and results in muscle that is refractory to future impulses. Cholinergic crisis also presents with muscle weakness; however, because the neuromuscular junction becomes insensitive to acetylcholine, edrophonium infusion produces no improvement in symptoms. AChE inhibitors should be temporarily discontinued in patients with cholinergic crisis **(Choice E)**.

**(Choice A)** Atropine is a muscarinic acetylcholine receptor antagonist that may be used in organophosphate poisoning and as a mydriatic agent (dilates pupils). However, it does not affect nicotinic receptors and is not used to treat myasthenic crisis.

**(Choice B)** Pralidoxime is also used in organophosphate poisoning. Pralidoxime reverses the effects of both muscarinic and nicotinic overstimulation by "regenerating" AChE in the neuromuscular junction.

**Educational objective:**
Exacerbation of myasthenia gravis in a patient treated with long-acting acetylcholinesterase inhibitors (eg, pyridostigmine) occurs due to myasthenic or cholinergic crisis. The edrophonium (Tensilon) test helps to differentiate these 2 conditions. Clinical improvement after edrophonium administration indicates that the


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junction becomes insensitive to acetylcholine, edrophonium infusion produces no improvement in symptoms. AChE inhibitors should be temporarily discontinued in patients with cholinergic crisis **(Choice E)**.

**(Choice A)** Atropine is a muscarinic acetylcholine receptor antagonist that may be used in organophosphate poisoning and as a mydriatic agent (dilates pupils). However, it does not affect nicotinic receptors and is not used to treat myasthenic crisis.

**(Choice B)** Pralidoxime is also used in organophosphate poisoning. Pralidoxime reverses the effects of both muscarinic and nicotinic overstimulation by "regenerating" AChE in the neuromuscular junction.

**Educational objective:**
Exacerbation of myasthenia gravis in a patient treated with long-acting acetylcholinesterase inhibitors (eg, pyridostigmine) occurs due to myasthenic or cholinergic crisis. The edrophonium (Tensilon) test helps to differentiate these 2 conditions. Clinical improvement after edrophonium administration indicates that the patient is undertreated (myasthenic crisis).

**References**

- Myasthenia gravis: a review.



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A 4-month-old boy is being evaluated for a hereditary metabolic disorder after presenting with failure to thrive and developmental delay. He was born outside the United States and had several seizures during the neonatal period. Physical examination reveals an abnormal head shape with a large anterior fontanelle and widely splayed cranial sutures. Profound hypotonia and hepatomegaly are also noted. Biochemical studies show elevated levels of very long chain fatty acids (VLCFAs) and phytanic acid. Cultured skin fibroblasts show impaired ability to oxidize VLCFAs. This patient's condition is best explained by dysfunction of which of the following cellular structures?

- A. Golgi apparatus
- B. Lysosomes
- C. Mitochondria
- D. Peroxisomes
- E. Proteasomes
- F. Rough endoplasmic reticulum


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thrive and developmental delay. He was born outside the United States and had several seizures during the neonatal period. Physical examination reveals an abnormal head shape with a large anterior fontanelle and widely splayed cranial sutures. Profound hypotonia and hepatomegaly are also noted. Biochemical studies show elevated levels of very long chain fatty acids (VLCFAs) and phytanic acid. Cultured skin fibroblasts show impaired ability to oxidize VLCFAs. This patient's condition is best explained by dysfunction of which of the following cellular structures?

A. Golgi apparatus (2%)
B. Lysosomes (12%)
C. Mitochondria (22%)
D. Peroxisomes (56%)
E. Proteasomes (3%)
F. Rough endoplasmic reticulum (1%)

Correct

56%

59 secs

12/31/2020



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| Functions of cellular organelles | |
|---|---|
| **Golgi apparatus** | • Protein modification, sorting & transport |
| **Lysosomes** | • Digestion of cellular debris & pathogens |
| **Mitochondria** | • TCA cycle & fatty acid oxidation<br>• Electron transport chain (ATP synthesis)<br>• Apoptosis |
| **Peroxisomes** | • Oxidation of very long & branched-chain fatty acids<br>• Hydrogen peroxide degradation |
| **Proteasomes** | • Degradation of ubiquitinated proteins |
| **Rough endoplasmic reticulum** | • Synthesis of integral membrane & secretory proteins |
| **Smooth endoplasmic reticulum** | • Drug detoxification<br>• Lipid, phospholipid & steroid synthesis |

Peroxisomal disorders are rare inborn errors of metabolism in which **peroxisomes** are either absent or


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| | |
|---|---|
| | • Lipid, phospholipid & steroid synthesis |

Peroxisomal disorders are rare inborn errors of metabolism in which **peroxisomes** are either absent or nonfunctional. **Very long chain fatty acids** (VLCFAs) and certain **branched-chain fatty acids** (eg, phytanic acid) cannot undergo mitochondrial beta-oxidation; these fatty acids are metabolized by a special form of beta-oxidation (VLCFAs) or by alpha-oxidation (branched-chain fatty acids) within peroxisomes. In peroxisomal disorders, these fatty acids build up in various tissues. Accumulation in neuronal cell membranes leads to **neurologic defects** due to improper neuronal migration, myelination, and degeneration.

This infant most likely has **Zellweger syndrome**, which is caused by defective peroxisomal biogenesis. It typically presents in early infancy with craniofacial abnormalities (eg, widened sutures, large anterior fontanelle), hepatomegaly, and profound neurologic defects (eg, hypotonia, seizures, developmental delay). Death usually occurs within months of initial presentation.

Another common peroxisomal disease is **X-linked adrenoleukodystrophy**, which is characterized by defective transport of VLCFAs into peroxisomes. Patients present in childhood or adulthood with neurologic deterioration and adrenal insufficiency as VLCFAs accumulate in the central nervous system and adrenal glands.


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and adrenal glands.

**(Choice A)** The Golgi apparatus is involved in posttranslational modification of proteins from the rough endoplasmic reticulum. It also routes proteins to their ultimate location (eg, lysosomes, extracellular space) using membrane-bound vesicles.

**(Choice B)** Lysosomes are organelles containing proteins that can digest a diverse range of biomolecules, cellular debris, and engulfed pathogens. Lysosomal storage disorders (eg, mucopolysaccharidoses, sphingolipidoses) result in intracellular accumulation of glycosaminoglycans, glycoproteins, or glycolipids.

**(Choice C)** Mitochondria are responsible for beta-oxidation of most fatty acids, ketogenesis, the TCA cycle and electron transport chain, and the first 2 steps of the urea cycle. Dysfunction can lead to various types of encephalomyopathy. Mitochondria do not metabolize VLCFAs or fatty acids with branch points at odd-numbered carbons.

**(Choice E)** Proteasomes degrade unneeded or defective intracellular proteins into small polypeptides or amino acids. Impaired proteasome function can lead to cell cycle dysregulation, protein aggregation, and defective processing of peptide antigens.

**(Choice F)** The rough endoplasmic reticulum is the site of synthesis for most secretory proteins, integral membrane proteins of the nucleus and cell membrane, and lysosomal proteins.



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**(Choice E)** Proteasomes degrade unneeded or defective intracellular proteins into small polypeptides or amino acids. Impaired proteasome function can lead to cell cycle dysregulation, protein aggregation, and defective processing of peptide antigens.

**(Choice F)** The rough endoplasmic reticulum is the site of synthesis for most secretory proteins, integral membrane proteins of the nucleus and cell membrane, and lysosomal proteins.

**Educational objective:**

The buildup of very long chain and branched-chain (eg, phytanic) fatty acids due to impaired oxidation is the hallmark of peroxisomal disorders (eg, Zellweger syndrome, adrenoleukodystrophy). Accumulation of these fatty acids in the brain results in permanent neurologic dysfunction.

**References**

- Peroxisome biogenesis disorders in the Zellweger spectrum: An overview of current diagnosis, clinical manifestations, and treatment guidelines.



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www.ncbi.nlm.nih.gov/pubmed/26750748

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A 23-year-old asymptomatic male participates in clinical research and is found to be homozygous for the apolipoprotein E-4 allele. In the future, this patient is most likely to suffer from which of the following?

A. Familial hypercholesterolemia
B. Hypertrophic cardiomyopathy
C. Diabetes mellitus, type 2
D. Peptic ulcer disease
E. Polycystic kidney disease
F. Alzheimer dementia

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A 23-year-old asymptomatic male participates in clinical research and is found to be homozygous for the apolipoprotein E-4 allele. In the future, this patient is most likely to suffer from which of the following?

A. Familial hypercholesterolemia (31%)
B. Hypertrophic cardiomyopathy (1%)
C. Diabetes mellitus, type 2 (3%)
D. Peptic ulcer disease (0%)
E. Polycystic kidney disease (1%)
✓ F. Alzheimer dementia (62%)

Correct

62%
Answered correctly

19 secs
Time Spent

01/30/2021
Last Updated

Explanation



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Alzheimer disease has a strong genetic predisposition. About 30% of patients have a family history of the disease. According to age when symptoms begin, Alzheimer disease can be classified as early or late.

The following three mutation sites have been associated with early-onset familial Alzheimer disease (onset <60 years old):

1. Amyloid precursor protein (APP) gene on chromosome 21
2. Presenilin 1 gene on chromosome 14
3. Presenilin 2 gene on chromosome 1

Both APP and presenilin gene mutations are thought to promote the production of A β-amyloid.

Late-onset familial Alzheimer disease is associated with the ε4 allele of Apolipoprotein E. The exact mechanism of its influence is not known. It is thought that the ApoE4 protein may be involved in the formation of senile plaques.

**(Choice A)** Familial hypercholesterolemia is an autosomal dominant disorder. It is associated with a defect in low-density lipoprotein (LDL) receptors. This defect leads to decreased hepatic LDL uptake and severe elevation in total cholesterol and LDL levels.

**(Choice B)** Hypertrophic cardiomyopathy is a familial disorder inherited as an autosomal dominant trait. The most common mutation is of the β-myosin heavy chain



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elevation in total cholesterol and LDL levels.

**(Choice B)** Hypertrophic cardiomyopathy is a familial disorder inherited as an autosomal dominant trait. The most common mutation is of the β-myosin heavy chain.

**(Choice C)** Genetic factors play an important role in diabetes mellitus type 2 (more important than in type 1). Genetic predisposition to increased insulin resistance and deranged insulin secretion by β-cells are important precursors to disease.

**(Choice D)** Peptic ulcer disease is strongly associated with *H. pylori* infection, but not ApoE4.

**(Choice E)** Polycystic kidney disease can be inherited as autosomal recessive (also called infantile form) or dominant trait (adult form). Neither of these conditions is associated with ApoE4.

**Educational Objective:**
Early-onset familial Alzheimer disease is associated with three gene mutations: APP (chromosome 21), presenilin 1 and presenilin 2. Late-onset familial Alzheimer disease is associated with apolipoprotein E4 genotype.

| Genetics | Nervous System | Alzheimer disease |
|---|---|---|
| Subject | System | Topic |


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A 26-year-old man is brought to the emergency department after a high-speed motorcycle collision. The patient was thrown several feet after his motorcycle collided with a car. On arrival, he is profoundly comatose. A CT scan of the head performed within an hour of the event shows no abnormalities. The patient dies several hours later, and autopsy examination is performed. Brain histopathology shows widespread axonal swelling, predominantly at the gray-white junction. Immunohistochemical staining of these axons reveals accumulation of alpha-synuclein and amyloid precursor proteins. Which of the following is the most likely cause of these observed findings?

A. Diffuse cerebral hypoperfusion
B. Disruption of the bridging cortical veins
C. Glutamate-mediated neuronal injury
D. Interruption of the white matter tracts
E. Secondary microvascular spasm

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- A. Diffuse cerebral hypoperfusion (28%)
- B. Disruption of the bridging cortical veins (5%)
- C. Glutamate-mediated neuronal injury (25%)
- D. Interruption of the white matter tracts (34%)
- E. Secondary microvascular spasm (5%)

Incorrect

34%

01 min, 12 secs

10/05/2020



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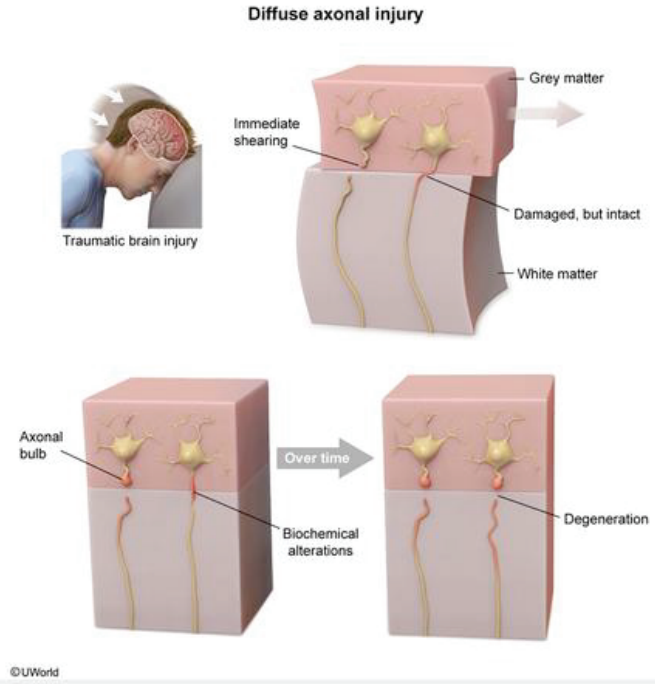


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This patient has histopathologic findings of **diffuse axonal injury** (DAI), a type of severe traumatic brain injury that can occur from direct blunt force injury (eg, head hitting windshield) or abrupt changes in acceleration-deceleration (eg, restrained passenger coming to sudden stop after a collision). Transfer of force can result in immediate **shearing of the white matter tracts** or induce secondary biochemical changes leading to degradation of the axonal cytoskeleton with subsequent axon breakage. Normal axonal transport is inhibited, leading to accumulation of axonally transported proteins (eg, **amyloid precursor**, **alpha-synuclein**) within axonal swellings at the point of injury (eg, axonal bulb formation).

Presentation varies based on the extent of injury; most patients are **comatose** (Glasgow Coma Score <8); however, those with very mild DAI may have only concussive symptoms (eg, headache, amnesia). CT scan has low sensitivity for diagnosis and is often normal, but MRI may demonstrate lesions at the gray-white junction. Microscopically, DAI is visible as **widespread axonal swelling**, most pronounced at the **gray-white matter junction**. Prognosis is poor, with up to 25% of cases resulting in death.

**(Choices A and C)** Diffuse cerebral hypoperfusion typically occurs in the setting of systemic hypotension or cardiac arrest. Watershed zone infarctions or diffuse edema with blurring of the gray-white junction are often visible on imaging. Ischemic neurons can release glutamate, leading to overactivation of the NMDA receptor with continuous membrane depolarization. This results in neuronal damage in a process known as excitotoxicity. Red neurons with intensely eosinophilic cytoplasm are seen on histopathology



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often visible on imaging. Ischemic neurons can release glutamate, leading to overactivation of the NMDA receptor with continuous membrane depolarization. This results in neuronal damage in a process known as excitotoxicity. Red neurons with intensely eosinophilic cytoplasm are seen on histopathology.

**(Choice B)** Disruption of the bridging cortical veins results in subdural hematoma; the elderly are at increased risk due to cerebral atrophy (stretching of the bridging veins increases the risk of tear). Subdural hematomas are visible on imaging as crescent-shaped hyperdensities that cross suture lines.

**(Choice E)** Subarachnoid hemorrhages are typically caused by rupture of saccular aneurysms but may be associated with trauma (typically with associated brain contusions); head CT scan demonstrates blood within the subarachnoid space.

**Educational objective:**

Diffuse axonal injury (DAI) is a type of traumatic brain injury that results from disruption of the white matter tracts. Microscopically, DAI is visible as widespread axonal swelling, most pronounced at the gray-white matter junction, with accumulation of transport proteins (eg, amyloid precursor, alpha-synuclein) at the site of injury.

**References**

- Axonal pathology in traumatic brain injury.



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A 28-year-old woman comes to the office due to pain at a previous surgery site. The patient underwent cesarean delivery a year ago and had no issues with wound healing. However, over the past 2 months, she has had intermittent sharp and burning pain at the incision site. Physical examination reveals a well-healed, low, transverse scar. There is a small knot palpable at the left end of the scar, light touch of which elicits severe pain. Cutaneous sensory nerve injury and abnormal axonal regeneration are suspected. Which of the following ion channels is most likely upregulated within the affected axons?

A. Calcium
B. Chloride
C. Magnesium
D. Potassium
E. Sodium

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A. Calcium (20%)
B. Chloride (3%)
C. Magnesium (0%)
D. Potassium (4%)
E. Sodium (70%)

Correct

70%
Answered correctly

02 mins, 15 secs
Time Spent

12/04/2020
Last Updated



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This patient likely suffered cutaneous nerve damage during her surgical procedure. Transected nerves undergo wallerian degeneration, which involves axonal dissolution while activated Schwann cells and macrophages degrade myelin. In addition to clearing cellular debris, Schwann cells and macrophages stimulate formation of a growth cone from the proximal axon stump to facilitate **nerve regeneration**. However, if the regenerating axons **cannot find their distal target**, regeneration can result in formation of a disorganized mass of axonal processes, Schwann cells, vascular hyalinization, and fibrosis known as a **neuroma**.

Chronic axonal injury or inflammation (such as occurs with a neuroma) induces increased expression of voltage-gated **sodium channels**, which are important for the generation and **propagation of action potentials**. The density of voltage-gated sodium channels correlates with the excitability of nerves; therefore, the upregulated sodium channels in injured nerves and neuromas increase nociceptive (pain) sensitivity.

To support the diagnosis of a neuroma, local anesthetic, which blocks sodium channels in the neuronal cell membrane, is administered to prevent depolarization of the nerve. This often provides immediate relief of pain.

**(Choice A)** Action potential propagation depends on voltage-gated calcium channels in certain cardiac



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This patient likely suffered cutaneous nerve damage during her surgical procedure. Transected nerves

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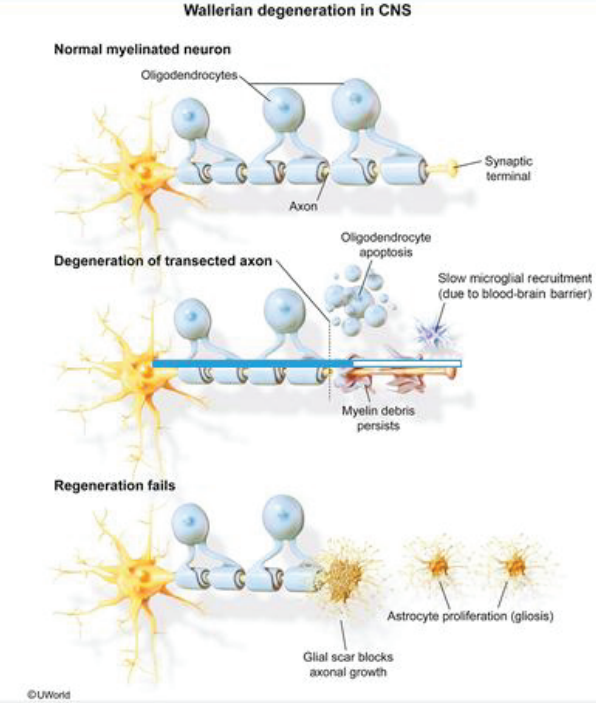


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This patient likely suffered cutaneous nerve damage during her surgical procedure. Transected nerves

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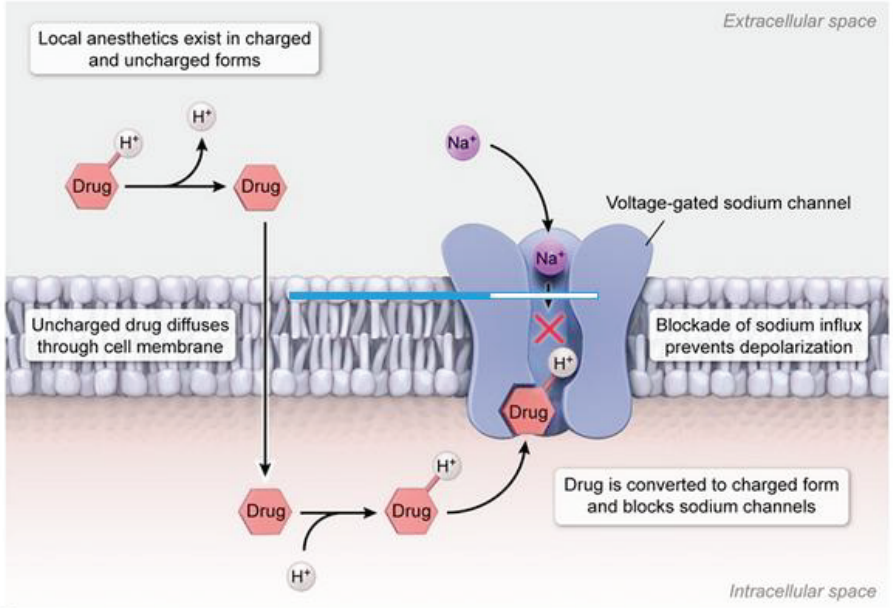
## Local anesthetic mechanism of action

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pain.

**(Choice A)** Action potential propagation depends on voltage-gated calcium channels in certain cardiac conduction tissues (eg, sinoatrial and atrioventricular nodes). However, peripheral nerve depolarization is driven primarily by sodium, rather than calcium, influx.

**(Choice B)** The influx of negative chloride ions often causes hyperpolarization, which inhibits formation of action potentials.

**(Choice C)** Magnesium selective ion channels are not directly involved in nerve depolarization. However, magnesium ions block calcium channels, preventing calcium influx at the axon terminal. This impairs release of neurotransmitter vesicles into the synapse, inhibiting impulse transmission.

**(Choice D)** The efflux of potassium out of the cell leads to hyperpolarization. Therefore, upregulation of potassium channels would tend to keep the membrane potential away from the depolarization threshold, leading to less signal transmission (ie, less pain).

**Educational objective:**

A neuroma forms when regenerating axons are unable to find their distal target and create a haphazard mass of axons and supporting cells. Upregulation of voltage-gated sodium channels, which generate and propagate action potentials, is likely responsible for the increased pain of these lesions.



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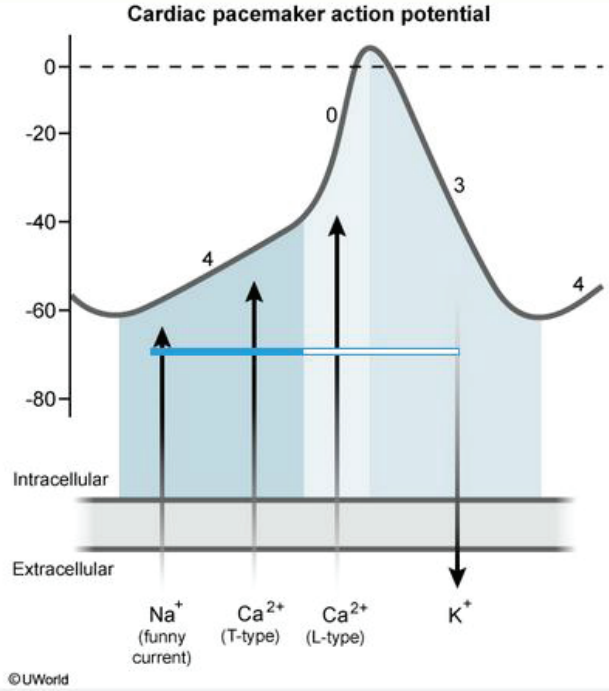


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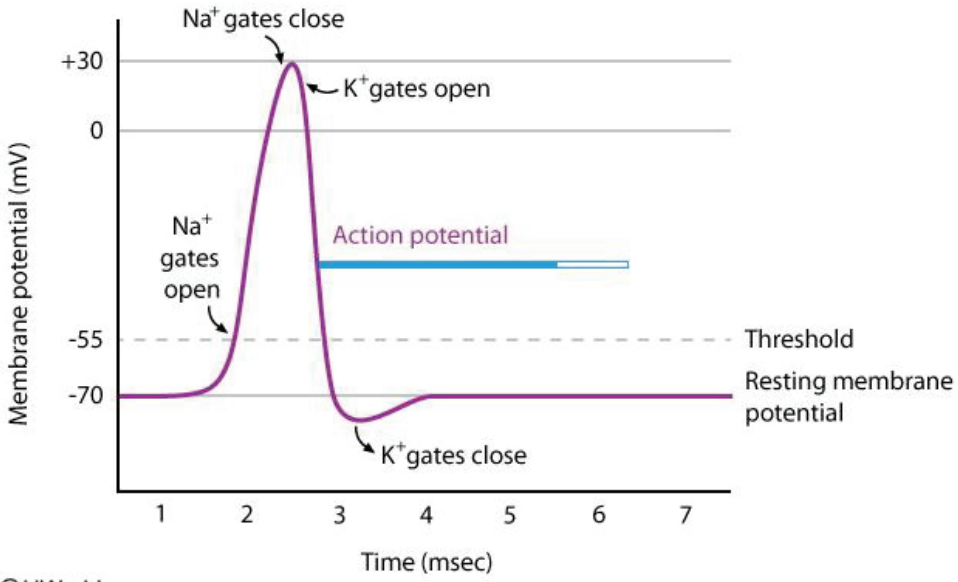
## Channel function during the action potential

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**(Choice D)** The efflux of potassium out of the cell leads to hyperpolarization. Therefore, upregulation of potassium channels would tend to keep the membrane potential away from the depolarization threshold, leading to less signal transmission (ie, less pain).

**Educational objective:**
A neuroma forms when regenerating axons are unable to find their distal target and create a haphazard mass of axons and supporting cells. Upregulation of voltage-gated sodium channels, which generate and propagate action potentials, is likely responsible for the increased pain of these lesions.

Pathophysiology Nervous System Neuronal physiology



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An elderly immigrant from the Middle East presents to your office complaining of numbness and tingling of his hands and feet. He was diagnosed with pulmonary tuberculosis several months ago and is currently receiving isoniazid and rifampin. Neurologic testing demonstrates sensory ataxia and decreased pain sensation in the distal extremities. This patient's condition is most likely caused by:

A. Immune-mediated demyelinization
B. Bacterial toxin-mediated axonal damage
C. Drug-mediated toxic neuron loss
D. Vitamin deficiency
E. Diabetic neuropathy

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An elderly immigrant from the Middle East presents to your office complaining of numbness and tingling of his hands and feet. He was diagnosed with pulmonary tuberculosis several months ago and is currently receiving isoniazid and rifampin. Neurologic testing demonstrates sensory ataxia and decreased pain sensation in the distal extremities. This patient's condition is most likely caused by:

A. ~~Immune-mediated demyelinization~~ (3%)
B. ~~Bacterial toxin-mediated axonal damage~~ (2%)
C. Drug-mediated toxic neuron loss (26%)
D. Vitamin deficiency (66%)
E. ~~Diabetic neuropathy~~ (1%)

Correct

66%
Answered correctly

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Explanation



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Isoniazid is chemically similar to pyridoxine (vitamin $B_6$). Because of this similarity, isoniazid can compete with vitamin $B_6$ in the synthesis of multiple neurotransmitters (including GABA), resulting in defective end products. Isoniazid also increases the urinary excretion of pyridoxine, and a frank deficiency of this vitamin can eventually develop. Vitamin $B_6$ deficiency most commonly occurs in patients treated with isoniazid who are elderly, alcoholics, or who have other comorbidities (eg, kidney or liver dysfunction). When isoniazid neuropathy occurs, it usually clinically manifests as peripheral neuropathy. To prevent these adverse effects, supplemental vitamin B6 is typically prescribed in conjunction with isoniazid.

**(Choice A)** Immune-mediated demyelinization occurs in multiple sclerosis and the Guillain-Barre syndrome. These conditions are not associated with antibiotic therapy of any kind.

**(Choice B)** Bacterial toxin-mediated axonal damage occurs in infections secondary to Corynebacterium diphtheriae, a microorganism that classically causes pseudomembranous pharyngitis. C. diphtheriae synthesizes a potent exotoxin associated with cardiac and neural toxicity.

**(Choice C)** Pyridoxine deficiency, not drug-mediated toxic neuron loss, is responsible for this patient's neuropathy. Drugs known to be directly toxic to nerves include the chemotherapeutic agents that inhibit microtubule formation (eg, vincristine and paclitaxel).

**(Choice E)** There is no evidence or clinical history suggestive of diabetic neuropathy in this patient. The


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**(Choice C)** Pyridoxine deficiency, not drug-mediated toxic neuron loss, is responsible for this patient's neuropathy. Drugs known to be directly toxic to nerves include the chemotherapeutic agents that inhibit microtubule formation (eg, vincristine and paclitaxel).

**(Choice E)** There is no evidence or clinical history suggestive of diabetic neuropathy in this patient. The primary cause of diabetic neuropathy is glucose-induced neural toxicity. High concentrations of glucose result in the formation of glycosylation products (eg, hemoglobin A1c) and the accumulation of sorbitol within the nerves, a phenomenon described as metabolic nerve damage.

**Educational Objective:**

Isoniazid is structurally similar to pyridoxine (vitamin $B_6$). As a result, this antibiotic increases the urinary excretion of pyridoxine – often causing a frank deficiency of vitamin $B_6$ — and competes for vitamin $B_6$-binding sites, leading to the defective synthesis of neurotransmitters like GABA. Isoniazid-induced neuropathy can usually be prevented with pyridoxine supplementation.

| Pharmacology | Nervous System | Tuberculosis |
|---|---|---|
| Subject | System | Topic |

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A 68-year-old woman is evaluated for right lower extremity weakness while hospitalized. The patient was admitted after sustaining a right femoral neck fracture and underwent total hip arthroplasty. Her operative course was uncomplicated, but the patient experienced right leg weakness postoperatively. Since the surgery, she has had difficulty with physical therapy and reports numbness of the right leg. The patient's other medical conditions include hypertension, type 2 diabetes mellitus, a prior transient ischemic attack, and osteoarthritis. Right lower extremity examination shows weakness in dorsiflexion, plantar flexion, and knee flexion. Hip flexion and knee extension are normal. Sensation to light touch is decreased on the dorsum of the right foot and posterolateral aspect of the right calf. Ankle reflex is absent on the right. Which of the following is the most likely cause of this patient's current findings?

A. Diabetic neuropathy
B. L5 radiculopathy
C. Lacunar stroke
D. Peroneal nerve compression
E. Sciatic nerve injury



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A. Diabetic neuropathy (2%)
B. L5 radiculopathy (12%)
C. Lacunar stroke (1%)
D. Peroneal nerve compression (24%)
E. Sciatic nerve injury (58%)

Correct

58%

01 min, 17 secs

10/25/2020



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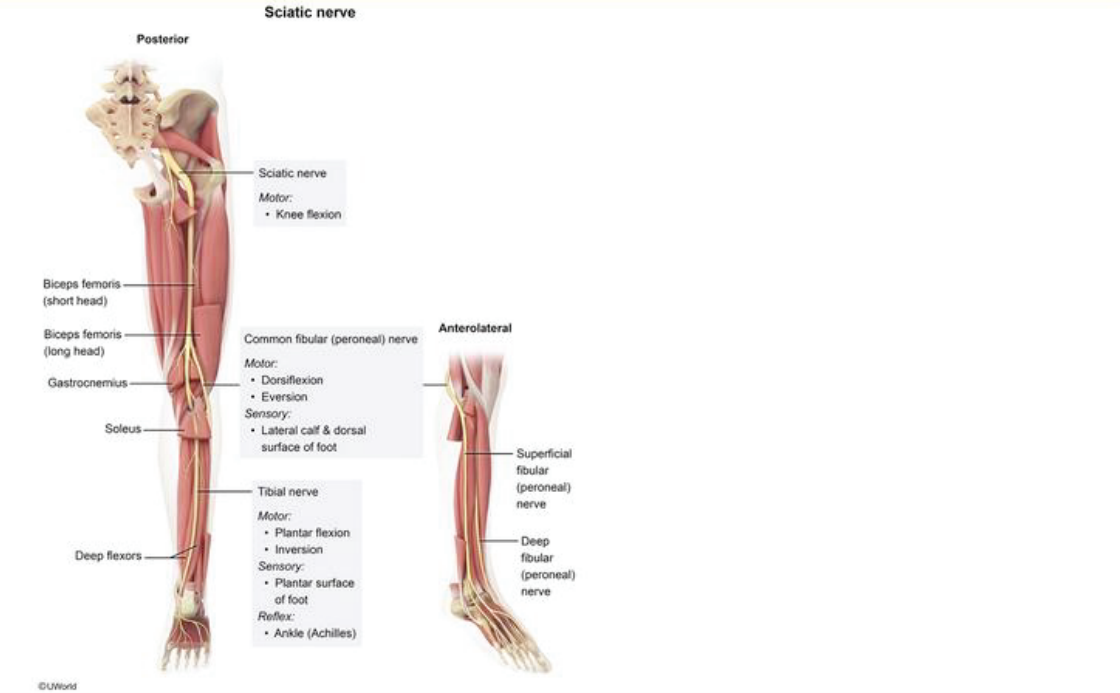


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This patient underwent total **hip replacement** following a right **femoral neck fracture** and developed **right lower extremity neurological deficits** across the sciatic nerve (L4-S3) and its main branches:

- Sciatic nerve: weakness in knee flexion
- Common peroneal nerve: weakness in dorsiflexion, numbness on dorsal foot and posterolateral calf
- Tibial nerve: weakness in plantar flexion and inversion, absent ankle reflex

These deficits are characteristic of a proximal **sciatic nerve injury**. The sciatic nerve is particularly susceptible to injury in patients with femoral head dislocation, hip fracture, and/or arthroplasty due to its **proximity to the hip joint** and femur. Injury to the nerve can be caused by direct mechanical trauma (caused by the surgery or initial fracture), compression of the nerve (due to hematoma or swelling), or local inflammation.

**(Choice A)** Diabetic neuropathy often manifests as peripheral sensory loss (eg, stocking-glove numbness). However, the deficits are typically bilateral and develop chronically with loss of distal sensory axons first, followed by motor deficits in advanced cases.

**(Choice B)** L5 radiculopathy is typically caused by disc herniation or degenerative vertebral changes and can result in unilateral lower extremity motor and sensory loss. However, patients typically have significant radicular back pain with a normal ankle reflex and lateral foot sensation (both derived from the S1 nerve


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**(Choice B)** L5 radiculopathy is typically caused by disc herniation or degenerative vertebral changes and can result in unilateral lower extremity motor and sensory loss. However, patients typically have significant radicular back pain with a normal ankle reflex and lateral foot sensation (both derived from the S1 nerve root).

**(Choice C)** Lacunar strokes occur in deep brain arteries in patients with chronic hypertension and typically cause unilateral sensorimotor deficits without cortical signs (eg, aphasia, hemineglect). However, these lesions typically result in more complete hemiparesis/hemisensory loss (eg, affecting face, arm, and leg); sensorimotor deficits localized to the sciatic distribution are more suggestive of peripheral nerve damage.

**(Choice D)** Compression of the common peroneal nerve against the neck of the fibula can occur in the setting of prolonged immobilization (eg, surgery, bed rest) and cause weakness in foot dorsiflexion and eversion. However, this patient also has deficits involving the sciatic and tibial nerves, indicating a more proximal lesion.

**Educational objective:**
Sciatic neuropathy is a common complication of hip fracture and/or arthroplasty because of the proximity of the sciatic nerve to the hip joint. Injury to the sciatic nerve in the pelvis causes neurological deficits across the sciatic nerve (knee flexion), common peroneal nerve (dorsiflexion, numbness of the calf and dorsal


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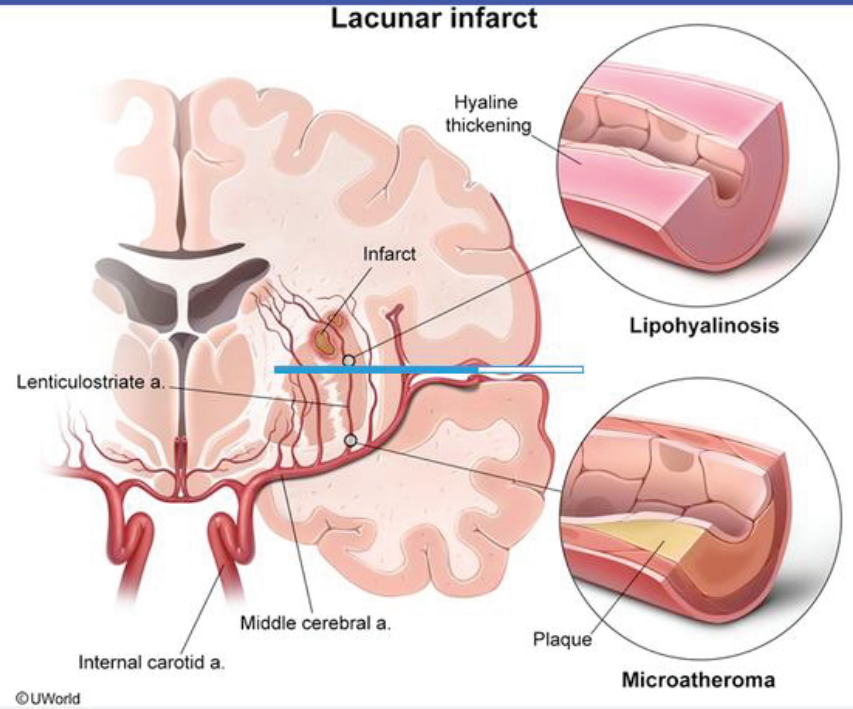


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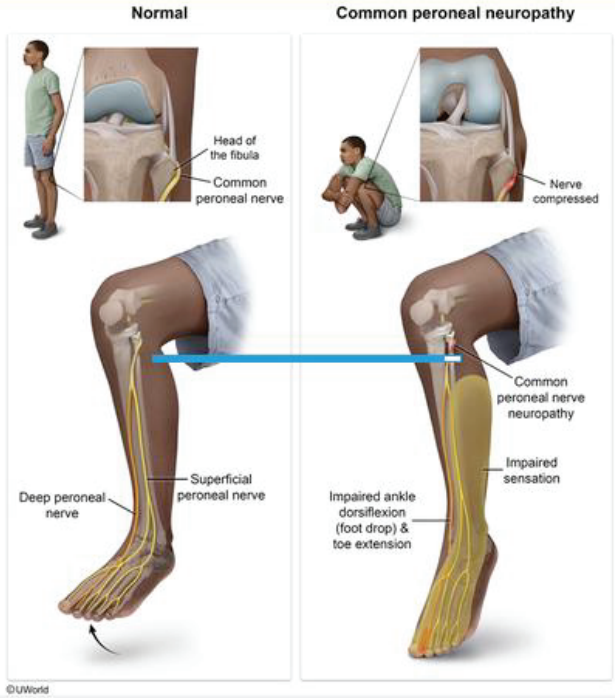


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**(Choice C)** Lacunar strokes occur in deep brain arteries in patients with chronic hypertension and typically cause unilateral sensorimotor deficits without cortical signs (eg, aphasia, hemineglect). However, these lesions typically result in more complete hemiparesis/hemisensory loss (eg, affecting face, arm, and leg); sensorimotor deficits localized to the sciatic distribution are more suggestive of peripheral nerve damage.

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**Educational objective:**

Sciatic neuropathy is a common complication of hip fracture and/or arthroplasty because of the proximity of the sciatic nerve to the hip joint. Injury to the sciatic nerve in the pelvis causes neurological deficits across the sciatic nerve (knee flexion), common peroneal nerve (dorsiflexion, numbness of the calf and dorsal foot), and tibial nerve (plantar flexion, ankle reflex).

| Anatomy | Nervous System | Sciatic neuropathy |
|---|---|---|
| Subject | System | Topic |



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A 74-year-old man with metastatic lung cancer is brought to the emergency department due to sudden-onset severe headache, nausea, and vomiting. The patient was diagnosed with squamous cell lung cancer 4 months ago and was found to have metastasis to the right frontal lobe of the brain. He refused chemotherapy and radiation treatments and is receiving palliative care. Blood pressure is 142/86 mm Hg, pulse is 100/min, and respirations are 20/min. On examination, the patient is somnolent but wakes up to voice and follows instructions. Urgent CT scan of the head reveals hemorrhage within the tumor, causing significant surrounding edema; the right cingulate gyrus is seen herniating beneath the falx cerebri. Which of the following findings is most likely to be present in this patient given his neuroimaging results?

A. Dilated and fixed right pupil
B. Left lower extremity weakness
C. Leftward conjugate eye deviation
D. Loss of gag and cough reflexes
E. Nonfluent/agrammatic speech


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onset severe headache, nausea, and vomiting. The patient was diagnosed with squamous cell lung cancer 4 months ago and was found to have metastasis to the right frontal lobe of the brain. He refused chemotherapy and radiation treatments and is receiving palliative care. Blood pressure is 142/86 mm Hg, pulse is 100/min, and respirations are 20/min. On examination, the patient is somnolent but wakes up to voice and follows instructions. Urgent CT scan of the head reveals hemorrhage within the tumor, causing significant surrounding edema; the right cingulate gyrus is seen herniating beneath the falx cerebri. Which of the following findings is most likely to be present in this patient given his neuroimaging results?

A. Dilated and fixed right pupil (30%)
B. Left lower extremity weakness (46%)
C. Leftward conjugate eye deviation (10%)
D. Loss of gag and cough reflexes (3%)
E. Nonfluent/agrammatic speech (8%)

Correct

46%
Answered correctly

01 min, 38 secs
Time Spent

11/08/2020
Last Updated



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| Clinical features of brain herniation | |
|---|---|
| **Herniation type** | **Common features** |
| **Subfalcine** | • Herniation of cingulate gyrus underneath falx cerebri<br>• No pupillary involvement, consciousness often preserved<br>• Contralateral leg weakness (ipsilateral ACA compression) |
| **Uncal** | • Herniation of uncus (medial temporal lobe) under tentorium cerebelli<br>• Ipsilateral dilated & fixed pupil (ipsilateral oculomotor nerve [CN III] compression)<br>• Early: contralateral hemiparesis (ipsilateral cerebral peduncle compression)<br>• Late: ipsilateral hemiparesis (contralateral cerebral peduncle compression) |
| **Central** | • Caudal displacement of diencephalon & brainstem<br>• Rupture of paramedian basilar artery branches<br>• Bilateral midposition & fixed pupils (loss of sympathetic & parasympathetic innervation)<br>• Decorticate (flexor) → decerebrate (extensor) posturing |


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| | • Decorticate (flexor) → decerebrate (extensor) posturing |
| **Tonsillar** | • Herniation of cerebellar tonsils through foramen magnum<br>• Coma, loss of CN reflexes, flaccid paralysis, respiratory arrest (brainstem compression) |

**ACA** = anterior cerebral artery; **CN** = cranial nerve.

**Brain herniation** occurs when an acute increase in intracranial pressure (ICP) causes a portion of the brain to protrude through an opening in the dural folds or foramen magnum. In this patient, mass effect from hemorrhage within the right frontal lobe metastasis is causing the **cingulate gyrus**, which is located at the medial aspect of the cerebral cortex just above the corpus callosum, to herniate **beneath the falx cerebri** (ie, subfalcine herniation).

Unlike in other herniation syndromes (eg, uncal, tonsillar), some **consciousness** is usually **preserved** in subfalcine herniation because there is no compression of brainstem wakefulness centers (eg, reticular activating system). Initial presentation may be as subtle as a headache; however, signs of increased ICP (eg, nausea, vomiting, lethargy) are often present, as in this patient. As it progresses, subfalcine herniation can cause **ipsilateral anterior cerebral artery compression**, leading to downstream ischemia and contralateral leg weakness.


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• Decorticate (flexor) → decerebrate (extensor) posturing

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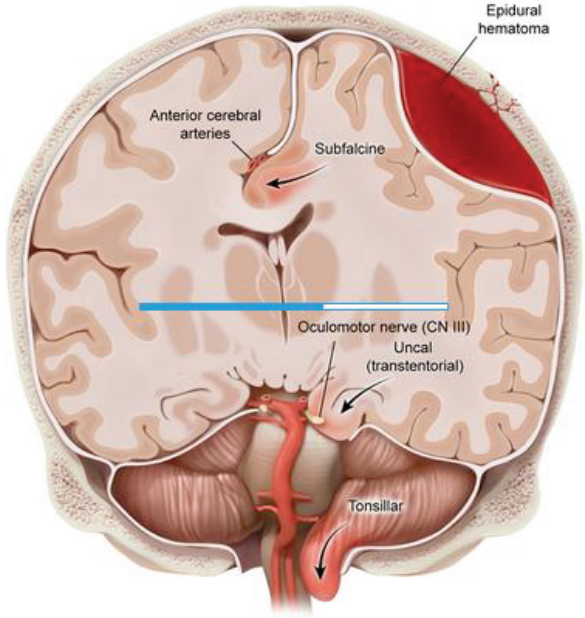
Types of brain herniation

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• Decorticate (flexor) → decerebrate (extensor) posturing

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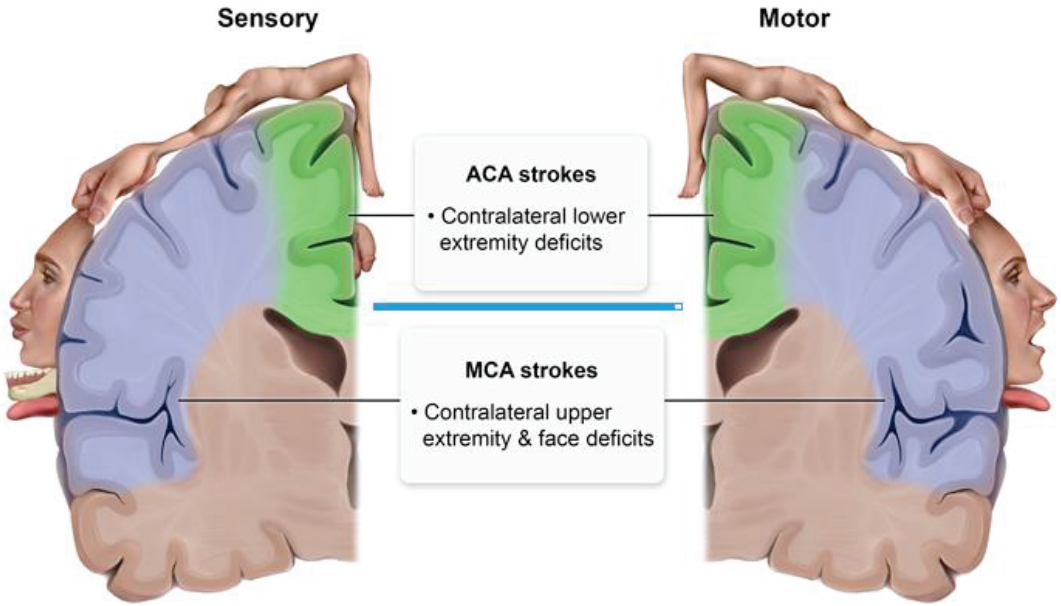
## Cerebral stroke patterns




**ACA** = anterior cerebral artery; **MCA** = middle cerebral artery.

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contralateral leg weakness.

**(Choice A)** A dilated and fixed right pupil may occur in uncal herniation due to compression of the ipsilateral oculomotor nerve (CN III). Uncal herniation involves herniation of the most medial portion of the temporal lobe (ie, uncus) beneath the tentorium cerebelli.

**(Choice C)** Conjugate eye deviation is a classic finding in middle cerebral artery (MCA) stroke. Resulting damage to the frontal eye field interrupts conjugate gaze, with the eyes directed toward the side of the lesion (eg, leftward gaze in left MCA stroke).

**(Choice D)** Loss of gag and cough reflexes may be seen with brainstem (eg, medulla) compression or injury, as can occur with acute herniation of the cerebellar tonsils through the foramen magnum.

**(Choice E)** Nonfluent/agrammatic speech (ie, expressive [motor] aphasia) is usually the result of injury to the Broca area, as can occur from a stroke involving the superior division of the dominant (typically left) middle cerebral artery.

**Educational objective:**
Subfalcine herniation occurs when the cingulate gyrus is displaced under the falx cerebri. Subfalcine herniation may compress the ipsilateral anterior cerebral artery, resulting in ischemia and contralateral leg weakness.



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contralateral leg weakness

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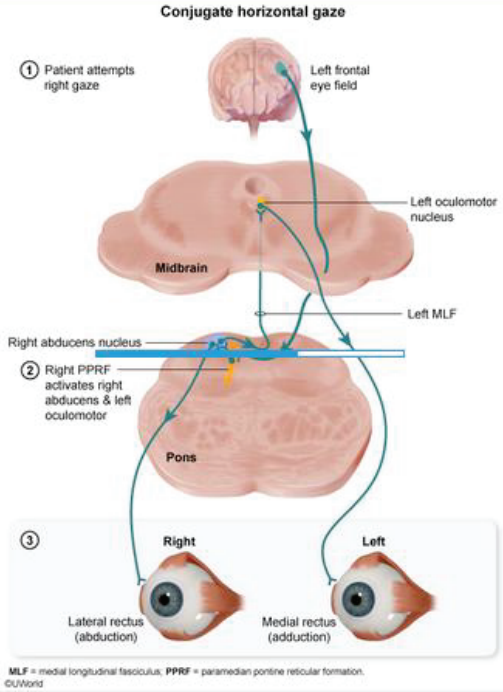


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contralateral leg weakness

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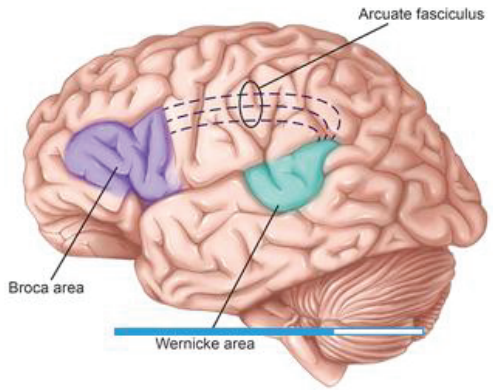
Common types of aphasia




| Aphasia syndrome | Spontaneous speech | Comprehension | Repetition | Associated features |
|---|---|---|---|---|
| Broca | Sparse & nonfluent | Relatively preserved | Impaired | Right hemiparesis (face & upper limb) |
| Wernicke | Fluent & voluminous but lacks meaning | Greatly diminished | Impaired | Right superior visual field defect |
| Conduction | Fluent with phonemic errors | Relatively preserved | Very poor | None |

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weakness.



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A 32-year-old man undergoes evaluation for episodes of paroxysmal supraventricular tachycardia. An electrophysiology study reveals focal atrial tachycardia that originates in the crista terminalis of the right atrium. Radiofrequency ablation is planned to destroy the ectopic focus and treat the arrhythmia. Which of the following nerves is in close proximity to the treatment site and is at risk for injury during the ablation?

A. Accessory nerve
B. Long thoracic nerve
C. Phrenic nerve
D. Recurrent laryngeal nerve
E. Sympathetic trunk

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A 32-year-old man undergoes evaluation for episodes of paroxysmal supraventricular tachycardia. An electrophysiology study reveals focal atrial tachycardia that originates in the crista terminalis of the right atrium. Radiofrequency ablation is planned to destroy the ectopic focus and treat the arrhythmia. Which of the following nerves is in close proximity to the treatment site and is at risk for injury during the ablation?

- A. ~~Accessory nerve~~ (1%)
- B. ~~Long thoracic nerve~~ (3%)
- ✓ C. Phrenic nerve (55%)
- D. Recurrent laryngeal nerve (29%)
- E. Sympathetic trunk (11%)

Correct

55%
Answered correctly

41 secs
Time Spent

03/14/2021
Last Updated

Explanation



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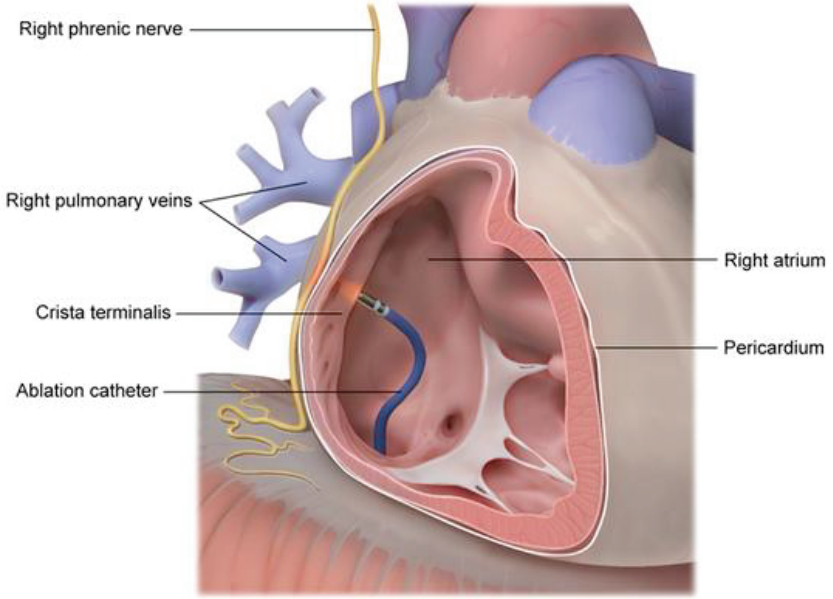
Phrenic nerve injury during catheter ablation

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**Paroxysmal supraventricular tachycardias** (PSVTs) are arrhythmias that occur intermittently and have abrupt onset and offset. They arise from regions of abnormal electrical activity that occur in the atrioventricular node, an accessory pathway, or the atria. **Radiofrequency ablation** can be used to destroy the inciting cardiomyocytes and cure the arrhythmia.

The crista terminalis, located in the **right atrium**, is a common site of origination for atrial PSVT. However, the **right phrenic nerve**, which innervates to the right hemidiaphragm, courses along the pericardium that overlies the right atrium and is at risk of injury during procedures that target structures in or near the right atrium (eg, crista terminalis, cavotricuspid isthmus, right-sided pulmonary veins). Such injury is typically recognized by **elevation of the right hemidiaphragm** on chest x-ray.

**(Choice A)** The spinal root of the accessory nerve (cranial nerve XI) courses superiorly from the upper spinal cord through the foramen magnum to join with the cranial root. The combined roots then exit the cranium through the jugular foramen to provide motor innervation to the sternocleidomastoid and trapezius muscles. There is risk of injury during biopsy or lymph node dissection in the neck, but not during procedures involving the right atrium.

**(Choice B)** The long thoracic nerve arises from the lower cervical spinal cord and courses laterally and



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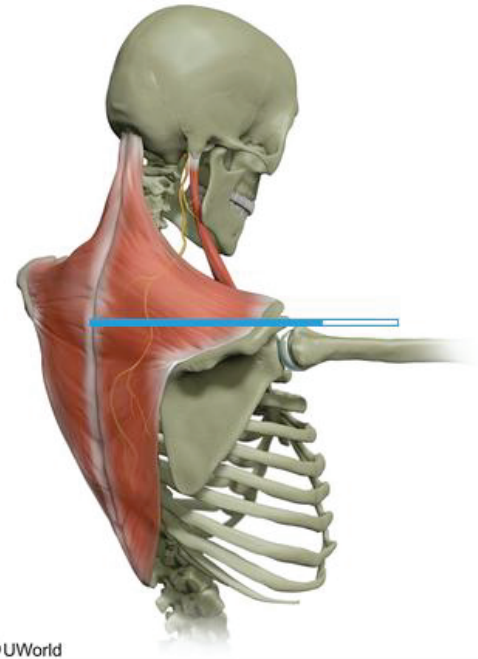


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(Choice B) The long thoracic nerve arises from the lower cervical spinal cord and courses laterally and



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**(Choice B)** The long thoracic nerve arises from the lower cervical spinal cord and courses laterally and inferiorly to provide motor innervation to the serratus anterior muscle. Injury can occur during breast surgery or chest-tube placement (resulting in a "winged" scapula); however, due to its lateral location, the nerve is not at risk of injury during procedures involving the right atrium.

**(Choice D)** The recurrent laryngeal nerve is a branch of the vagus nerve (cranial nerve X) that courses underneath the aortic arch on the left and the brachiocephalic trunk on the right to provide motor, sensory, and parasympathetic innervation to the upper esophagus, trachea, and portions of the larynx. It is at risk of injury during thyroid surgery but not during procedures involving the right atrium.

**(Choice E)** The sympathetic trunk parallels the length of the spinal column on both sides and provides sympathetic innervation throughout the body. Injury leads to Horner syndrome (ie, miosis, ptosis, anhydrosis) and can occur during spinal surgery, but not during procedures involving the right atrium.

**Educational objective:**
The right phrenic nerve courses along the pericardium overlying the right side of the heart and is at risk for injury during procedures in or near the right atrium (eg, radiofrequency ablation). Right phrenic nerve injury is typically recognized by elevation of the right hemidiaphragm.



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(Choice B) The long thoracic nerve arises from the lower cervical spinal cord and courses laterally and

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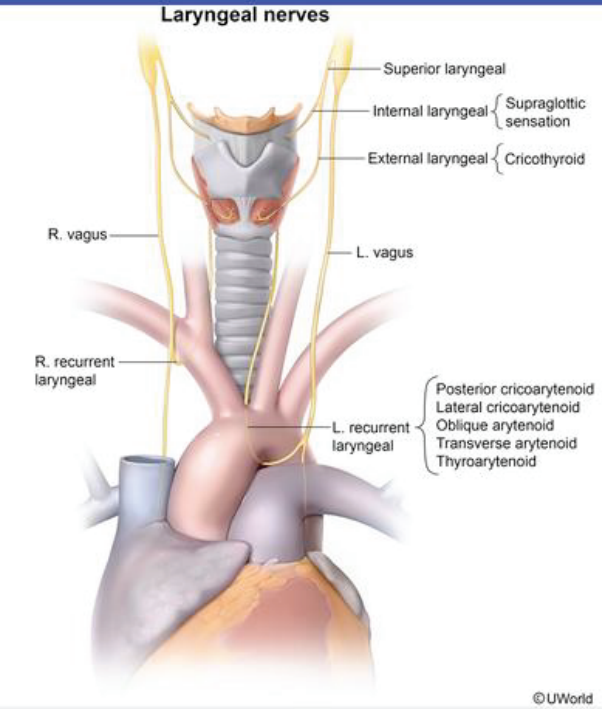


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A 4-day-old premature infant in the neonatal intensive care unit becomes hypotonic and less responsive. She was delivered vaginally at 30 weeks gestation, and her birth weight was 1,200 g (2 lb 10 oz). Physical examination shows a lethargic infant with weak and high-pitched crying, prominent scalp veins, and tense fontanelles. Cranial ultrasound reveals blood in the lateral ventricles. Which of the following structures is the most likely source of the bleeding?

A. Bridging cortical veins
B. Germinal matrix
C. Meningeal arteries
D. Sagittal sinus
E. Vessels of the circle of Willis

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A 4-day-old premature infant in the neonatal intensive care unit becomes hypotonic and less responsive. She was delivered vaginally at 30 weeks gestation, and her birth weight was 1,200 g (2 lb 10 oz). Physical examination shows a lethargic infant with weak and high-pitched crying, prominent scalp veins, and tense fontanelles. Cranial ultrasound reveals blood in the lateral ventricles. Which of the following structures is the most likely source of the bleeding?

A. Bridging cortical veins (13%)
B. Germinal matrix (60%)
C. Meningeal arteries (5%)
D. Sagittal sinus (13%)
E. Vessels of the circle of Willis (7%)

Correct

60%
Answered correctly

10 secs
Time Spent

02/09/2021
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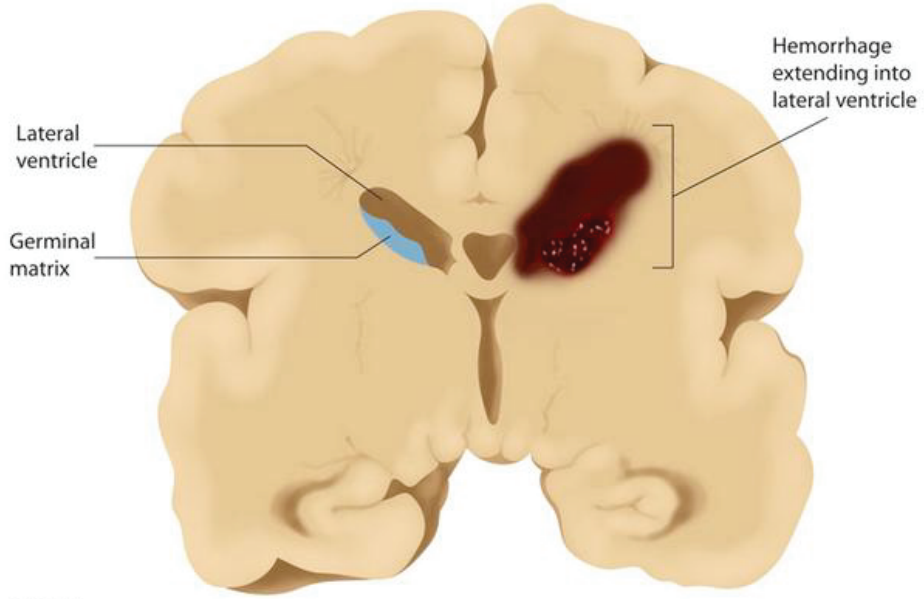
Exhibit Display

## Germinal matrix hemorrhage

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**Intraventricular hemorrhage (IVH)** is a common complication of prematurity that can lead to long-term impairment in neurodevelopment. IVH almost always manifests within the first 5 postnatal days in infants born **before 32 weeks gestation** and/or with **birth weight <1,500 g** (3 lb 5 oz). IVH in a newborn can be clinically silent or present with altered level of consciousness, hypotonia, and decreased spontaneous movements. If the bleeding is severe, catastrophic deterioration can occur with a **bulging anterior fontanelle**, hypotension, tonic-clonic seizures, irregular respirations, and coma.

IVH in preterm infants usually originates from the **germinal matrix**, a highly cellular and vascularized layer in the subventricular zone (source of neurons and glial cells during brain development). The matrix contains numerous fragile, thin-walled vessels lacking the glial fibers that support other blood vessels throughout the brain, making them more **susceptible to hemorrhage**. Between 24-32 weeks gestation, the germinal matrix starts to become less prominent, and its cellularity and vascularity decrease, leading to a reduced risk of IVH in infants born after 32 weeks.

**(Choices A and C)** In neonates, an assisted delivery (eg, forceps, vacuum) can result in subdural hematoma (cortical bridging veins) or epidural hematoma (middle meningeal artery). Both can cause bulging fontanelles and altered level of consciousness but are characterized by hematomas over the



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**(Choices A and C)** In neonates, an assisted delivery (eg, forceps, vacuum) can result in subdural hematoma (cortical bridging veins) or epidural hematoma (middle meningeal artery). Both can cause bulging fontanelles and altered level of consciousness but are characterized by hematomas over the cerebral convexities rather than blood in the lateral ventricles.

**(Choice D)** The sagittal sinus and other dural venous sinuses are channels found between layers of dura mater in the brain. Certain conditions (eg, malignancy, hypercoagulable states, infection) can result in thrombosis within the dural sinuses; however, intraventricular bleeding would not be seen.

**(Choice E)** A ruptured saccular (berry) aneurysm at a branch point in vessels of the circle of Willis is the most common cause of spontaneous subarachnoid hemorrhage (SAH). Aneurysmal SAH is rare in infants and is associated with blood in the basal cisterns rather than the lateral ventricles.

**Educational objective:**
Neonatal intraventricular hemorrhage usually originates from the fragile germinal matrix in infants born before 32 weeks gestation and/or with birth weight <1,500 g (3 lb 5 oz). It is a common complication of prematurity that can lead to long-term neurodevelopmental impairment.

| Anatomy | Nervous System | Intraventricular hemorrhage |
|---|---|---|
| Subject | System | Topic |



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A 19-year-old man is brought to the emergency department after sustaining a traumatic brain injury during a motor vehicle collision. On arrival, the patient is comatose and has a Glasgow Coma Scale score of 3. His blood pressure is 110/70 mm Hg, and pulse is 114/min. Pupils are miotic, equal, and reactive to light. Ecchymosis is present behind the ear, but the remainder of the trauma survey is unremarkable. Rapid-sequence intubation is performed, and the patient is mechanically ventilated. A noncontrast head CT scan demonstrates bifrontal contusions and a basilar skull fracture. One day later, a repeat head CT scan reveals diffuse cerebral edema. The ventilator respiratory rate is adjusted to achieve a $PaCO_2$ level of 26-30 mm Hg. Which of the following is the most likely effect of this intervention?

A. Decreased brain metabolic demand
B. Increased cerebral perfusion
C. Increased cerebral blood volume
D. Increased cerebral vascular resistance
E. Increased displacement of cerebrospinal fluid into the thecal sac



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a motor vehicle collision. On arrival, the patient is comatose and has a Glasgow Coma Scale score of 3. His blood pressure is 110/70 mm Hg, and pulse is 114/min. Pupils are miotic, equal, and reactive to light. Ecchymosis is present behind the ear, but the remainder of the trauma survey is unremarkable. Rapid-sequence intubation is performed, and the patient is mechanically ventilated. A noncontrast head CT scan demonstrates bifrontal contusions and a basilar skull fracture. One day later, a repeat head CT scan reveals diffuse cerebral edema. The ventilator respiratory rate is adjusted to achieve a $PaCO_2$ level of 26-30 mm Hg. Which of the following is the most likely effect of this intervention?

A. Decreased brain metabolic demand (12%)
B. Increased cerebral perfusion (19%)
C. Increased cerebral blood volume (1%)
✓ D. Increased cerebral vascular resistance (61%)
E. Increased displacement of cerebrospinal fluid into the thecal sac (5%)

Correct
61%
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10/19/2020


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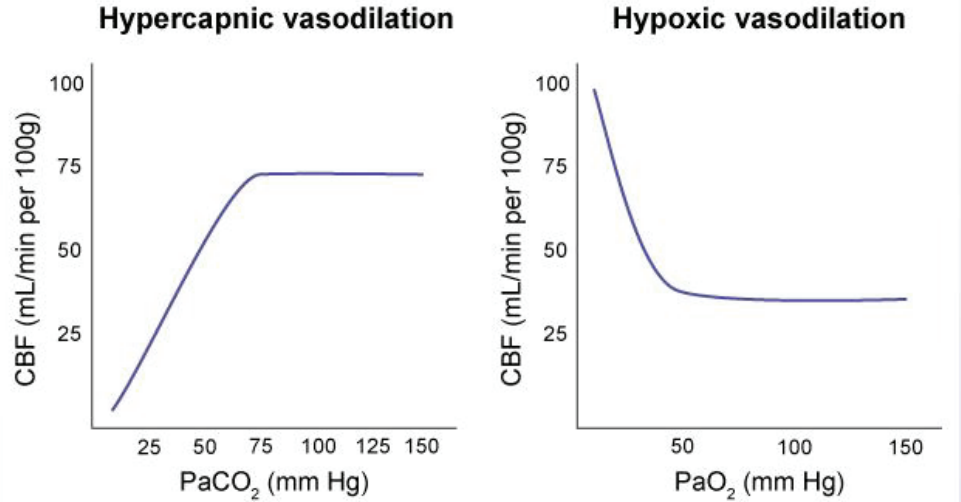


**CBF** = cerebral blood flow.

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The brain has little room for expansion as it is encased in the cranium. A small volume change in any of the intracranial components (eg, brain tissue, blood, cerebrospinal fluid [CSF]) can produce significant changes in intracranial pressure (ICP). Therefore, even small increases in cerebral blood volume can raise ICP and cause brain compression.



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The main factors influencing cerebral circulation are systemic blood pressure and arterial blood gas levels. When systemic blood pressure is 60-140 mm Hg, it has little effect on cerebral blood volume because autoregulation (via cerebral blood vessel dilation and contraction) keeps blood flow constant. Blood pressure >150 mm Hg increases cerebral vascular volume and blood flow, causing a corresponding increase in ICP. In contrast, blood pressure <50 mm Hg causes cerebral hypoperfusion and potential ischemia.

Arterial blood gases also have a powerful effect on cerebral blood flow, with $PaCO_2$ being the most important regulator. A **drop in $PaCO_2$** due to hyperventilation causes **vasoconstriction**. The resulting reduction in cerebral blood volume **(Choice C)** leads to decreased ICP. Lowering $PaCO_2$ is one of the measures employed to **reduce ICP** in mechanically ventilated patients with cerebral edema.

**(Choice A)** The brain has a very large oxygen requirement, about 20% of all $O_2$ consumed by the body. Induced sedation and therapeutic hypothermia can decrease brain metabolic demand, exerting a neuroprotective effect and improving ICP by reducing cerebral blood volume.

**(Choice B)** The vasoconstriction induced by hyperventilation can cause a decrease in local cerebral perfusion that can worsen neurologic injury in patients with acute traumatic brain injury or stroke.



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Induced sedation and therapeutic hypothermia can decrease brain metabolic demand, exerting a neuroprotective effect and improving ICP by reducing cerebral blood volume.

**(Choice B)** The vasoconstriction induced by hyperventilation can cause a decrease in local cerebral perfusion that can worsen neurologic injury in patients with acute traumatic brain injury or stroke. Therefore, hyperventilation should be used with caution in these patients, and the $PaCO_2$ should be maintained $\geq$30 mm Hg.

**(Choice E)** The thecal sac is a sheath of dura mater that contains CSF and surrounds the spinal cord. Increased ICP can cause displacement of CSF from the brain into the thecal sac. However, the drop in ICP caused by hyperventilation reduces CSF displacement.

**Educational objective:**
Carbon dioxide is a potent vasodilator of cerebral vasculature. Tachypnea causes hypocapnia and cerebral vasoconstriction, thereby decreasing cerebral blood volume and intracranial pressure.

| Physiology | Nervous System | Traumatic brain injury |
|---|---|---|
| Subject | System | Topic |

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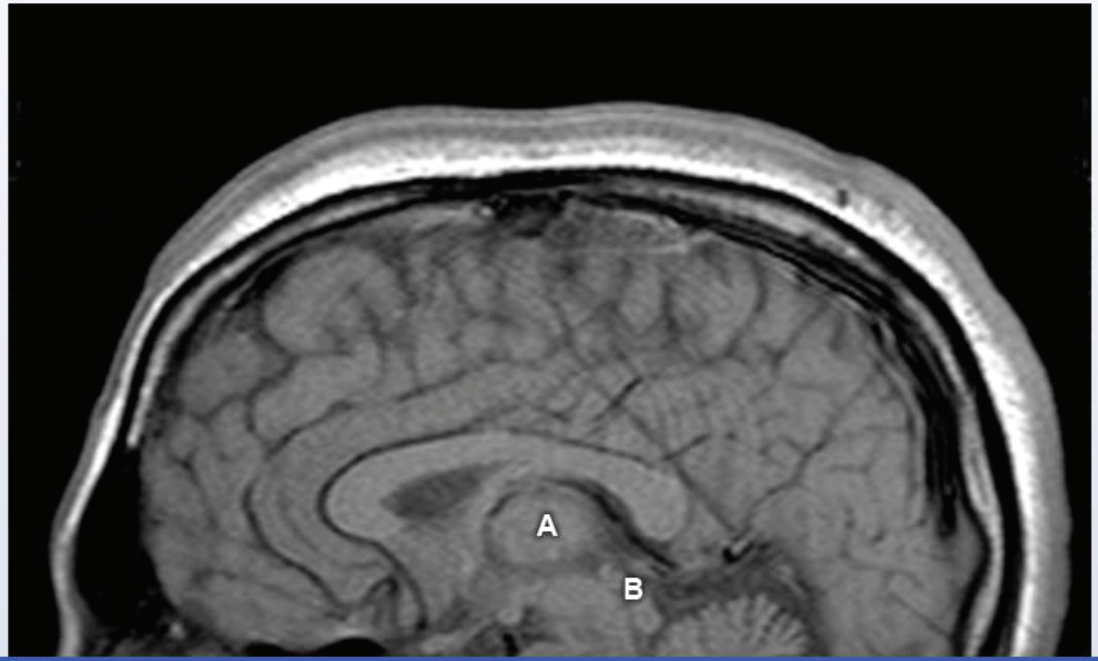
A 34-year-old man begins treatment with combination chemotherapy for Hodgkin lymphoma. Shortly thereafter, he experiences severe vomiting and requires intravenous fluid supplementation. Which of the following sites in the brain is most likely responsible for his symptoms?



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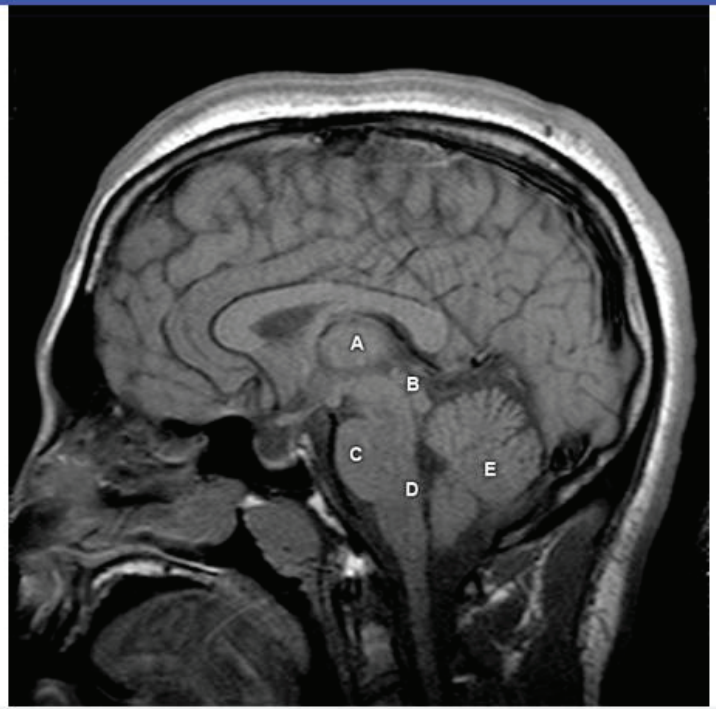


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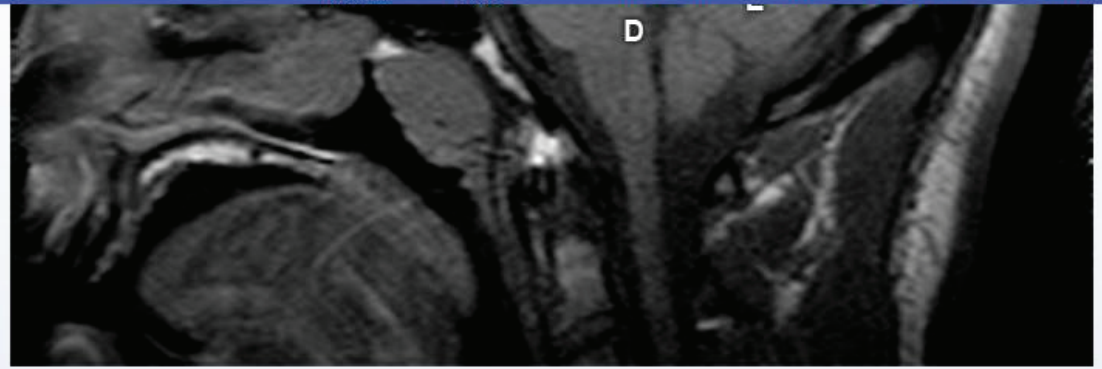


- A.A
- B.B
- C.C
- D.D
- E.E

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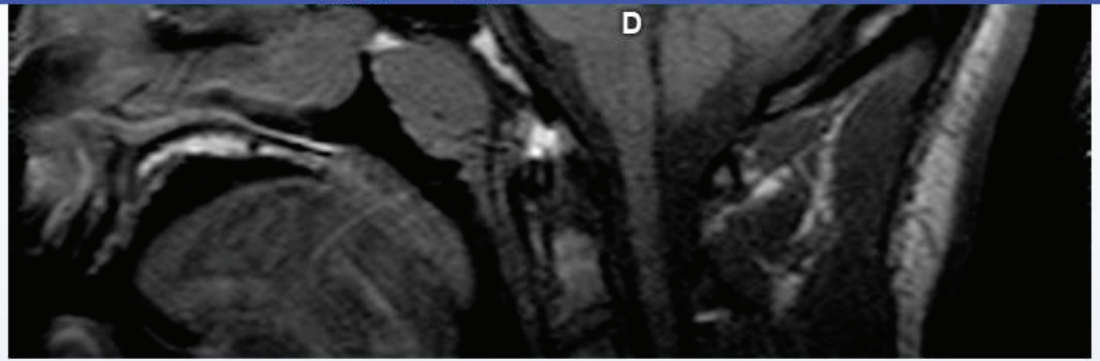


- A.A (10%)
- B.B (13%)
- C.C (8%)
- ✓ D.D (64%)
- E.E (3%)

Correct

64%

01 min, 11 secs

02/28/2021



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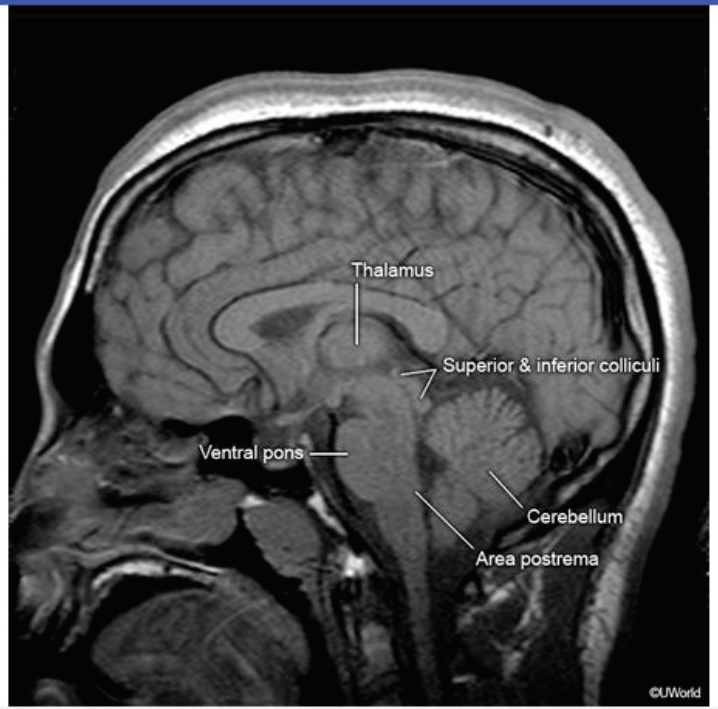


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This patient developed acute vomiting after treatment with systemic chemotherapy. The vomiting reflex is initiated by the **chemoreceptor trigger zone** (CTZ, or area postrema) and nucleus tractus solitarius. The **area postrema** is located on the dorsal surface of the medulla at the caudal end of the fourth ventricle; this region does not have a well-developed blood-brain barrier, allowing it to be exposed to chemicals circulating in the blood.

The CTZ can be triggered directly by emetogenic substances (eg, drugs, toxins) or indirectly by vagal afferents from the gastrointestinal tract. **Chemotherapeutic agents** (eg, cyclophosphamide) cause damage to enterocytes, resulting in release of serotonin. This stimulates **5-HT3 receptors** on vagal afferent fibers located in the bowel wall, which then ascend to the CTZ to trigger the **vomiting reflex**. Chemotherapy-associated emetic stimuli in the cerebrospinal fluid and bloodstream also can stimulate the area postrema directly by causing local release of substance P, which activates **neurokinin-1 (NK1) receptors** in the brainstem to induce vomiting.

Selective 5-HT3 receptor antagonists (eg, ondansetron) and NK1 receptor antagonists (eg, aprepitant, fosaprepitant) can be used to ameliorate chemotherapy-induced nausea and vomiting by reducing overstimulation of the CTZ.

**(Choice A)** The thalamus is superior to the midbrain and makes up part of the lateral wall of the third ventricle. It coordinates sensory and motor function, regulates sleep and wakefulness, and plays an


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overstimulation of the CTZ.

**(Choice A)** The thalamus is superior to the midbrain and makes up part of the lateral wall of the third ventricle. It coordinates sensory and motor function, regulates sleep and wakefulness, and plays an important role in memory and cognition.

**(Choice B)** The superior and inferior colliculi are located in the dorsal midbrain. They are involved in processing visual (superior colliculi) and auditory (inferior colliculus) information and initiating movement of the head and eyes in response to visual or auditory input.

**(Choice C)** The ventral pons is inferior to the midbrain in the brainstem and contains the corticospinal tract (eg, limb/torso movement), corticobulbar tract (eg, face/head/neck movement), and abducens nucleus (eg, horizontal eye movement).

**(Choice E)** The cerebellum makes up the posterior wall of the fourth ventricle and plays an important role in motor control (eg, coordination, precise movements, posture) and cognitive function (eg, attention, language).

**Educational objective:**

The vomiting reflex is initiated by the chemoreceptor trigger zone (ie, area postrema) and nucleus tractus solitarius within the dorsal medulla at the caudal end of the fourth ventricle. The area postrema does not



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**(Choice C)** The ventral pons is inferior to the midbrain in the brainstem and contains the corticospinal tract (eg, limb/torso movement), corticobulbar tract (eg, face/head/neck movement), and abducens nucleus (eg, horizontal eye movement).

**(Choice E)** The cerebellum makes up the posterior wall of the fourth ventricle and plays an important role in motor control (eg, coordination, precise movements, posture) and cognitive function (eg, attention, language).

**Educational objective:**

The vomiting reflex is initiated by the chemoreceptor trigger zone (ie, area postrema) and nucleus tractus solitarius within the dorsal medulla at the caudal end of the fourth ventricle. The area postrema does not have a well-developed blood brain barrier, allowing it to be activated directly by emetogenic substances (eg, drugs, toxins) or indirectly by ascending afferents from the bowel wall (eg, chemotherapy-induced release of serotonin).

**References**

- Physiology, Chemoreceptor Trigger Zone

| Anatomy | Nervous System | Nausea and vomiting |
|---|---|---|
| Subject | System | Topic |



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A 32-year-old woman comes to the emergency department due to severe headache, nausea, and vomiting for the past several hours. The headache is pounding and localized to the left side. She also describes bright spots in her vision prior to headache onset. The patient has had similar episodes occasionally since adolescence. Physical examination shows normal pupils and fundi, but the patient has discomfort to bright light. There is no facial droop, extremity weakness, or sensory loss. The patient is treated with metoclopramide and diphenhydramine. Which of the following is the most likely reason diphenhydramine was used in this patient?

A. To decrease the risk of arrhythmia
B. To increase the prokinetic effect
C. To prevent abnormal motor reaction
D. To prevent allergic reaction
E. To prevent rebound headache

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A. To decrease the risk of arrhythmia (2%)
B. To increase the prokinetic effect (11%)
C. To prevent abnormal motor reaction (47%)
D. To prevent allergic reaction (12%)
E. To prevent rebound headache (26%)

47%  21 secs  10/30/2020



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| Common antiemetic drugs | | | |
|---|---|---|---|
| **Drug class** | **Examples** | **Clinical uses** | **Major side effects** |
| **Antimuscarinics (anticholinergics)** | • Scopolamine | • Vestibular nausea<br>• Motion sickness | • Anticholinergic effects (eg, dry mouth, sedation) |
| **Antihistamines** | • Meclizine | | |
| **Dopamine receptor antagonists (DRAs)** | • Prochlorperazine<br>• Metoclopramide<br>• Chlorpromazine | • Migraine headache (DRAs)<br>• Acute or chronic nausea/vomiting<br>• Acute chemotherapy-induced emesis | • Extrapyramidal reactions |
| **Serotonin (5-$HT_3$) receptor antagonists** | • Ondansetron<br>• Granisetron | | • QT prolongation |
| **Neurokinin-1 (NK1) receptor antagonists** | • Aprepitant<br>• Fosaprepitant | • Delayed chemotherapy-induced emesis | • Neutropenia |



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| | | induced emesis | |
|---|---|---|---|

This patient with a normal neurologic examination has unilateral headache associated with **nausea and vomiting**, photophobia, and a visual aura (eg, flashing lights), features that are consistent with **migraine headache**.

Severe migraine headache with nausea and vomiting is typically treated with a serotonin 1B/1D agonist (ie, triptans) or a **dopamine receptor blocker** (eg, metoclopramide, prochlorperazine) to abort the migraine and treat associated nausea and vomiting. Dopamine receptor blockers have both antiemetic and analgesic effects on migraine headaches by antagonizing central dopamine **D2 receptors** in the midbrain and striatum.

Dopamine receptor blockade in the basal ganglia can also cause **excess cholinergic activity** that manifests as significant **extrapyramidal symptoms**, such as **acute dystonic reaction** (eg, torticollis, oculogyric crisis). Therefore, **diphenhydramine** can be co-administered with metoclopramide or prochlorperazine to prevent such reactions due to its **anticholinergic activity**.

**(Choice A)** The $5HT_3$ receptor antagonists ondansetron and granisetron have a low risk of QT prolongation leading to torsade de pointes. However, administration of diphenhydramine does not decrease this risk.


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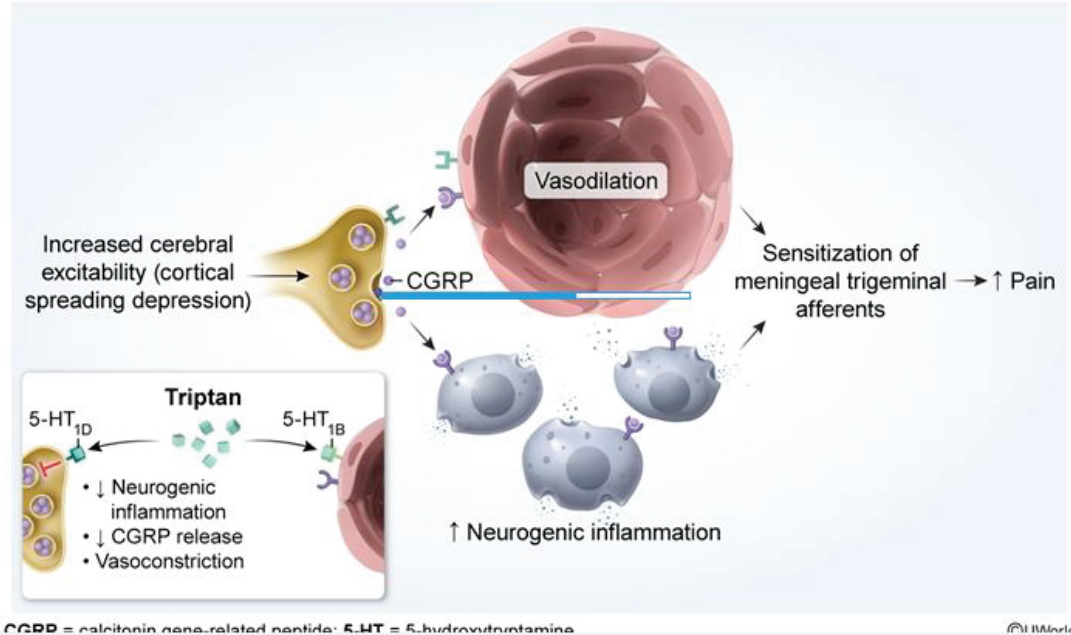
induced emesis

Exhibit Display

## Migraine pathogenesis & triptan mechanism of action




CGRP = calcitonin gene-related peptide; 5-HT = 5-hydroxytryptamine

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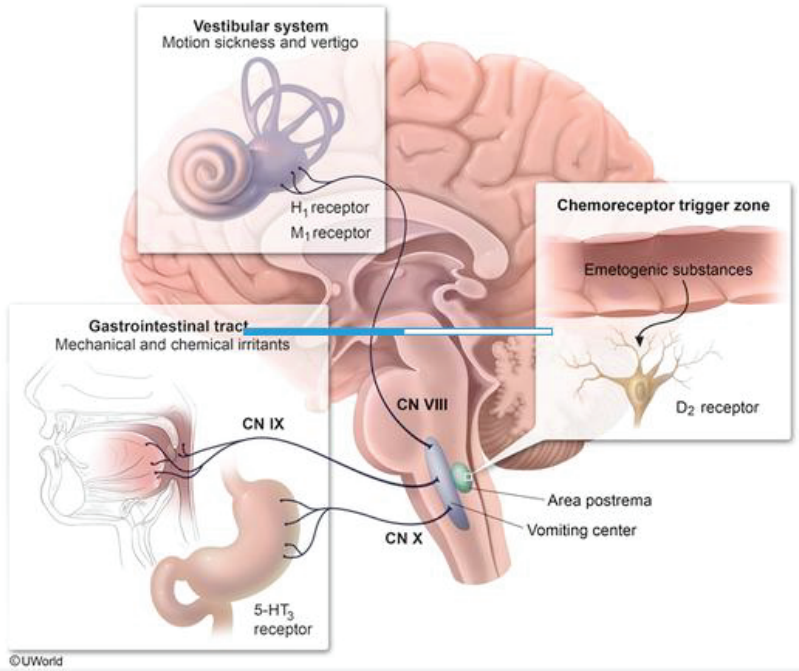
induced emesis

Exhibit Display

Physiologic causes of nausea

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decrease this risk.

**(Choice B)** Metoclopramide has prokinetic activity (eg, enhances gastric emptying) and can be useful in the treatment of nausea and vomiting associated with diabetic gastroparesis. However, administration of diphenhydramine would decrease this prokinetic effect due to its anticholinergic activity (eg, reduced gut motility).

**(Choice D)** Diphenhydramine is a first-generation (H1) antihistamine used to treat urticaria, which can occur with allergic drug reactions. However, it is not used to prevent occurrence of allergic reactions.

**(Choice E)** Rebound headache can occur with excessive use (eg, >10 days a month) of certain abortive migraine medications (eg, triptans, analgesics). Dopamine receptor antagonists are not typically associated with rebound headache.

**Educational objective:**
Dopamine receptor blockers (eg, metoclopramide, prochlorperazine) act as antiemetics and pain relievers for severe migraine headache associated with nausea and vomiting. However, dopamine blockade can also result in excess cholinergic activity (eg, acute dystonic reactions); diphenhydramine can be co-administered with dopamine receptor blockers to prevent these reactions due to its anticholinergic activity.

**References**


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A 43-year-old woman comes to the office due to acute back pain after dragging a heavy box. The pain is located in her lower back and radiates down the right posterior thigh to the foot. The patient describes the pain as "shooting" and grades it 8/10 in intensity. She has no bowel or bladder symptoms. The patient has tried over-the-counter analgesics with limited symptomatic relief. Vital signs are within normal limits. On physical examination, straight leg raise testing is positive on the right. Right hip extension is weaker when compared to the left. Knee jerk reflexes are 2+ and bilaterally symmetric, but the right ankle jerk reflex is absent. Which of the following nerve roots is most likely affected in this patient?

- A. L2
- B. L3
- C. L4
- D. L5
- E. S1

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- A. L2 (3%)
- B. L3 (2%)
- C. L4 (9%)
- D. L5 (13%)
- ✓ E. S1 (70%)

70%  01 min, 22 secs  01/11/2021



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**Features of lumbosacral radiculopathy**

| Nerve Root | Reflex affected | Sensory loss* | Weakness |
|---|---|---|---|
| **L2-L4**** | • Patellar | • Anteromedial thigh<br>• Medial shin | • Hip flexion (iliopsoas)<br>• Hip adduction<br>• Knee extension (quadriceps) |
| **L5** | • None | • Lateral shin<br>• Dorsum of the foot | • Foot dorsiflexion & inversion (tibialis anterior)<br>• Foot eversion (peroneus)<br>• Toe extension (extensor hallucis and digitorum) |
| **S1** | • Achilles | • Posterior calf<br>• Sole & lateral foot | • Hip extension (gluteus maximus)<br>• Foot plantarflexion (gastrocnemius) |
| **S2-S4**** | • Anocutaneous | • Perineum | • Urinary or fecal incontinence<br>• Sexual dysfunction |



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| | | | |
|---|---|---|---|
| | | | • Sexual dysfunction |

*Radicular pain typically has a similar distribution to sensory loss.

** Difficult to distinguish between individual nerve roots clinically.

This patient's presentation is consistent with **sciatica**, a nonspecific term for low back pain that radiates down the leg. This condition occurs due to compression of the lumbosacral nerve roots and is most commonly caused by vertebral disc herniation or spinal foraminal stenosis (eg, due to degenerative arthritis of the spine). Irritation of the nerve roots results in characteristic dermatomal and myotomal deficits (radiculopathy) depending on the level of involvement. Patients may have worsening of their radicular pain when the symptomatic leg is extended at the knee and the hip is passively flexed by the examiner (straight leg raise test).

The sciatic nerve is derived from the L4-S3 nerve roots and compression most often occurs at the level of L5 or S1. **S1 radiculopathy** is characterized by pain and sensory loss down the posterior thigh and calf to the lateral aspect of the foot. Patients may also have **weakness** on **thigh extension** (eg, due to denervation of the gluteus maximus), knee flexion (hamstrings), and foot plantarflexion (gastrocnemius) with an **absent ankle jerk reflex**. Conversely, compression of the L5 root results in pain/paresthesia radiating down the lateral thigh and calf to the dorsal foot. Patients often have weakness on foot


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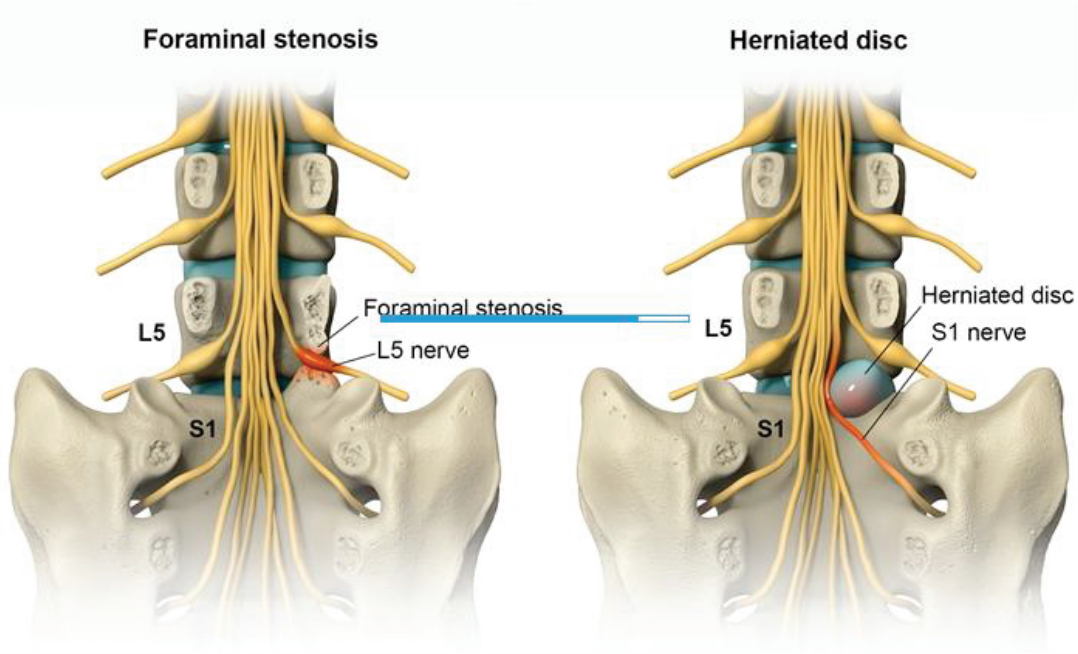
- Sexual dysfunction

Exhibit Display

## Lumbosacral degenerative disease

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- Sexual dysfunction

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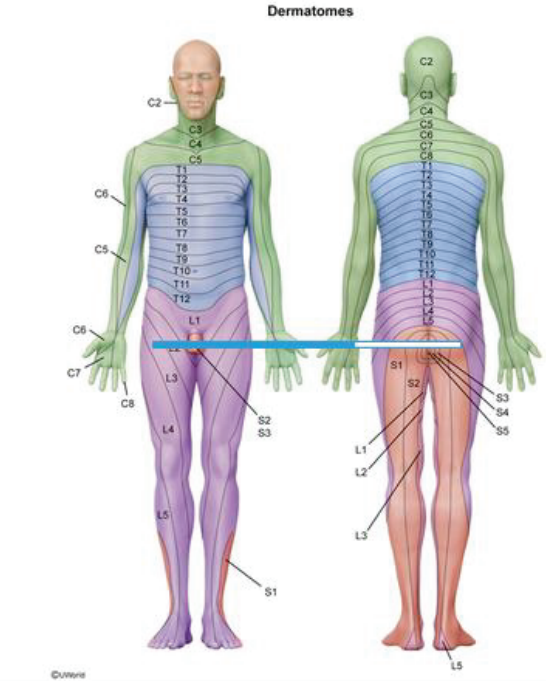


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with an **absent ankle jerk reflex**. Conversely, compression of the L5 root results in pain/paresthesia radiating down the lateral thigh and calf to the dorsal foot. Patients often have weakness on foot dorsiflexion and inversion (eg, due to denervation of the tibialis anterior), foot eversion (peroneus), and toe extension (extensor digitorum brevis) **(Choice D)**.

**(Choices A and B)** Patients with L2 or L3 radiculopathy typically have pain radiating down the anterior thigh with weakness on hip flexion (eg, due to denervation of the iliopsoas). Knee and ankle jerk reflexes usually remain intact.

**(Choice C)** L4 radiculopathy typically presents with pain/paresthesia radiating down the anterior thigh to the medial lower leg and foot. Patients can also have weakness on knee extension (eg, due to denervation of the quadriceps) with a diminished knee jerk reflex.

**Educational objective:**
Sciatica is a nonspecific term for low back pain that radiates down the leg due to compression of the lumbosacral nerve roots (eg, from vertebral disc herniation). The S1 nerve root is commonly involved, resulting in pain/sensory loss down the posterior thigh and calf to the lateral aspect of the foot. Patients may also have weakness on thigh extension, knee flexion, and foot plantarflexion with an absent ankle jerk reflex.


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A 44-year-old man comes to the office due to several weeks of difficulty walking and frequent falls. He has had no headache or visual impairment but reports episodes of sharp, stabbing pain in his extremities. The patient has HIV acquired from unprotected sexual contact and is nonadherent with treatments. Temperature is 37 C (98.6 F). Neurologic examination shows 5/5 motor power in all extremities. Deep-tendon reflexes are absent at the knee and ankle bilaterally. Proprioception and vibration sensation are reduced throughout the lower extremities. He has a wide-based gait and a positive Romberg sign. Which of the following diagnostic findings is most likely associated with this patient's current symptoms?

A. Cerebrospinal fluid (CSF) culture growing acid-fast bacilli
B. CSF PCR positive for herpes virus
C. Encapsulated yeasts on CSF India ink preparation
D. Polyomavirus-infected glial cells on brain biopsy
E. Reactive VDRL tests on CSF samples
F. Ring-enhancing lesions on brain MRI


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had no headache or visual impairment but reports episodes of sharp, stabbing pain in his extremities. The patient has HIV acquired from unprotected sexual contact and is nonadherent with treatments. Temperature is 37 C (98.6 F). Neurologic examination shows 5/5 motor power in all extremities. Deep-tendon reflexes are absent at the knee and ankle bilaterally. Proprioception and vibration sensation are reduced throughout the lower extremities. He has a wide-based gait and a positive Romberg sign. Which of the following diagnostic findings is most likely associated with this patient's current symptoms?

A. Cerebrospinal fluid (CSF) culture growing acid-fast bacilli (2%)
B. CSF PCR positive for herpes virus (3%)
C. Encapsulated yeasts on CSF India ink preparation (4%)
D. Polyomavirus-infected glial cells on brain biopsy (13%)
E. Reactive VDRL tests on CSF samples (65%)
F. Ring-enhancing lesions on brain MRI (10%)

Correct

65%

01 min, 29 secs

02/03/2021



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| Tabes dorsalis | |
|---|---|
| **Epidemiology** | • Years → decades after initial infection<br>• Increased incidence/more rapid progression in those with HIV |
| **Pathogenesis** | • *Treponema pallidum* directly damages dorsal sensory roots<br>• Secondary degeneration of the dorsal columns |
| **Clinical findings** | • Sensory ataxia<br>• Lancinating pains<br>• Neurogenic urinary incontinence<br>• Associated with Argyll Robertson pupils |
| **Treatment** | • 10-14 days of intravenous penicillin G |

This patient's sensory ataxia and lancinating pains raises suspicion for **tabes dorsalis**, a late form of **neurosyphilis** that usually manifests several years or decades after initial infection with *Treponema pallidum*. Tabes dorsalis is characterized by a slow degeneration of nerve fibers in the **dorsal column** of the spinal cord and **dorsal nerve roots**, which leads to diminished vibratory, proprioception, and



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*pallidum*. Tabes dorsalis is characterized by a slow degeneration of nerve fibers in the **dorsal column** of the spinal cord and **dorsal nerve roots**, which leads to diminished vibratory, proprioception, and discriminative touch sensation.

Common manifestations include:

- **Sensory ataxia**: Wide-based gait and loss of equilibrium when the patient's eyes are closed (positive Romberg sign); due to damaged lower extremity proprioception
- Absent deep-tendon reflexes: Due to damaged dorsal nerve roots
- **Lancinating pains**: Sharp, stabbing pains that may last minutes or hours; the exact cause is unclear

Spirochetal damage to the midbrain tectum also commonly results in **Argyll Robertson pupil**. This finding is marked by small, irregularly shaped pupils that fail to constrict to light but that constrict normally to accommodation (light-near dissociation). Most patients with tertiary syphilis will have a **positive VDRL** and mild lymphocytic pleocytosis on cerebrospinal fluid analysis.

**(Choice A)** Central nervous system infection with *Mycobacterium tuberculosis*, an acid-fast bacillus, is usually characterized by headache, vomiting, cranial nerve deficits, and confusion. Lancinating pains and altered lower extremity sensation would be atypical.


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altered lower extremity sensation would be atypical.

**(Choice B)** Herpes simplex encephalitis primarily affects the temporal lobe and causes fever, headache, impaired consciousness, and seizures.

**(Choice C)** Cryptococcal meningitis can be diagnosed by examining the cerebrospinal fluid for encapsulated yeasts using India ink. However, cryptococcal meningitis usually manifests with fever, malaise, and headache. Lancinating pains, absent deep-tendon reflexes, and altered sensation would be atypical.

**(Choice D)** JC virus is a polyomavirus that replicates in oligodendrocytes (glial cells). Reactivation of JC virus causes progressive multifocal leukoencephalopathy, which occurs primarily in severely immunocompromised patients (eg, AIDS, lymphoma, leukemia) and causes progressive dementia, motor deficits, and visual impairment.

**(Choice F)** Patients with untreated HIV are at high risk for cerebral toxoplasmosis, which usually manifests with headache, confusion, fever, and focal neurologic deficits. MRI of the brain usually reveals ring-enhancing lesions.

**Educational objective:**
Tabes dorsalis, a late form of neurosyphilis, causes progressive degeneration of the dorsal columns and


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atypical.

**(Choice D)** JC virus is a polyomavirus that replicates in oligodendrocytes (glial cells). Reactivation of JC virus causes progressive multifocal leukoencephalopathy, which occurs primarily in severely immunocompromised patients (eg, AIDS, lymphoma, leukemia) and causes progressive dementia, motor deficits, and visual impairment.

**(Choice F)** Patients with untreated HIV are at high risk for cerebral toxoplasmosis, which usually manifests with headache, confusion, fever, and focal neurologic deficits. MRI of the brain usually reveals ring-enhancing lesions.

**Educational objective:**

Tabes dorsalis, a late form of neurosyphilis, causes progressive degeneration of the dorsal columns and dorsal roots of the spinal cord. Manifestations include loss of proprioception and vibratory sensation, severe lancinating pains, and sensory ataxia (eg, wide-based gait, positive Romberg sign). Many patients also have Argyll Robertson pupils.

**References**

- REVIEW: Neurosyphilis: a historical perspective and review.



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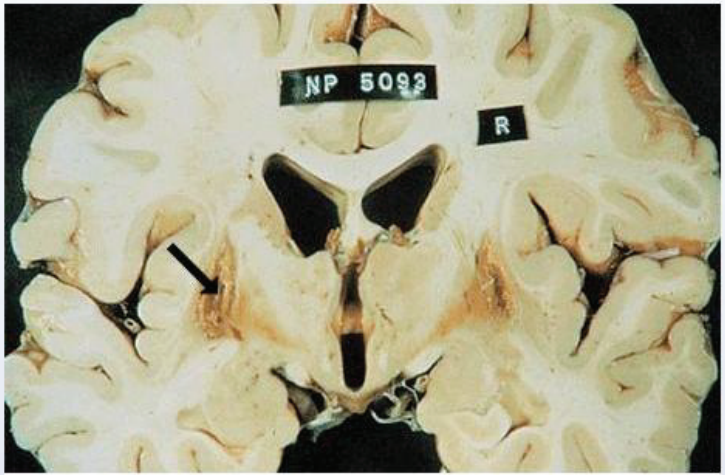
A 54-year-old Caucasian male dies from a progressive neurological disorder. A brain section of the patient is shown below.

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Which of the following corresponds to the structure with cystic degeneration (black arrow)?

A. Globus pallidus



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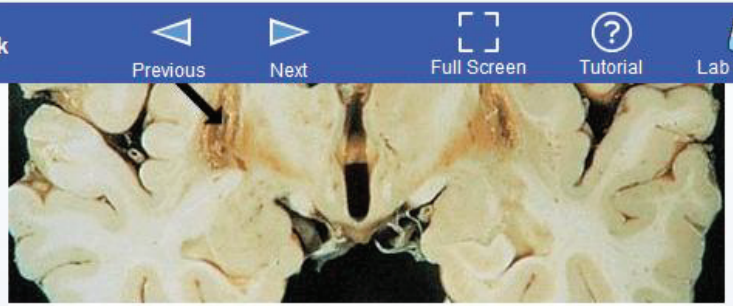

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Which of the following corresponds to the structure with cystic degeneration (black arrow)?

- A. Globus pallidus
- B. Putamen
- C. Internal capsule
- D. Caudate nucleus
- E. Amygdala

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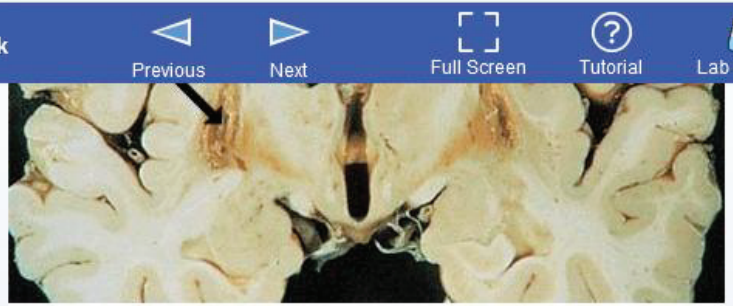

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Which of the following corresponds to the structure with cystic degeneration (black arrow)?

- A. Globus pallidus (18%)
- ✓ B. Putamen (54%)
- C. Internal capsule (8%)
- D. Caudate nucleus (15%)
- E. Amygdala (2%)

Correct

54%

36 secs

12/23/2020



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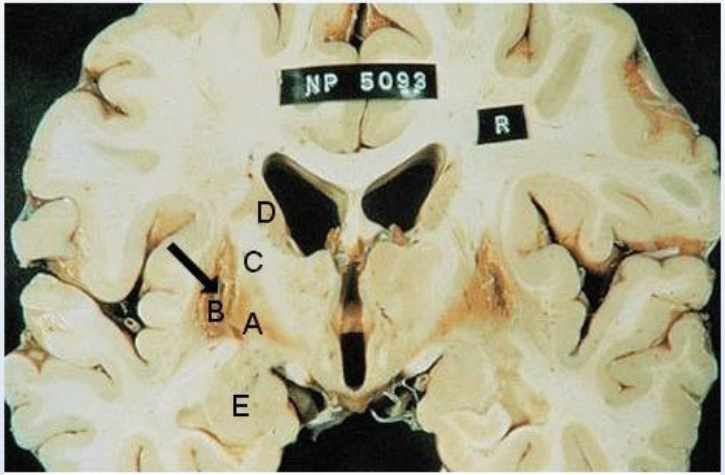
Many progressive neurologic diseases may be associated with cystic degeneration of the putamen, but Wilson's disease is the most likely of these to be emphasized on the USMLE.

The putamen **(Choice B)** can be identified on coronal sections (either in gross specimens as above or on imaging studies) in a location immediately deep (medial) to the insula and lateral to the globus pallidus and internal capsule.

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**(Choice A)** The globus pallidus is the orange-colored structure on the above image immediately medial to the degenerated putamen. It is considered part of the basal ganglia along with the caudate and putamen.

**(Choice C)** The internal capsule is the white matter structure that separates the globus pallidus and putamen from the caudate nucleus anteriorly and from the thalamus posteriorly on coronal sections.

**(Choice D)** In its full three dimensional structure, the caudate nucleus is a curved or "C-shaped" structure that can be identified in the inferolateral walls of the anterior horns of the lateral ventricles. However, only a small cross-section is visible in the image above next to the lateral ventricles. This structure is affected in Huntington's disease.

**(Choice E)** The amygdala is a group of neurons in the medial temporal lobe located adjacent to the hippocampus that plays a role in the limbic system. The amygdala can be identified on the image above as the circular grey matter structures in the medial temporal lobe immediately inferior to the globus pallidus and putamen. The amygdala mediates fear and some sympathetic stimulation in humans.

**Educational Objective:**
Wilson's disease can cause cystic degeneration of the putamen as well as damage to other basal ganglia structures. The putamen is located medial to the insula and lateral to the globus pallidus on coronal



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putamen from the caudate nucleus anteriorly and from the thalamus posteriorly on coronal sections.

**(Choice D)** In its full three dimensional structure, the caudate nucleus is a curved or "C-shaped" structure that can be identified in the inferolateral walls of the anterior horns of the lateral ventricles. However, only a small cross-section is visible in the image above next to the lateral ventricles. This structure is affected in Huntington's disease.

**(Choice E)** The amygdala is a group of neurons in the medial temporal lobe located adjacent to the hippocampus that plays a role in the limbic system. The amygdala can be identified on the image above as the circular grey matter structures in the medial temporal lobe immediately inferior to the globus pallidus and putamen. The amygdala mediates fear and some sympathetic stimulation in humans.

**Educational Objective:**
Wilson's disease can cause cystic degeneration of the putamen as well as damage to other basal ganglia structures. The putamen is located medial to the insula and lateral to the globus pallidus on coronal sections.

| Anatomy | Nervous System | Wilson disease |
|---|---|---|
| Subject | System | Topic |



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A 27-year-old woman comes to the office due to almost daily headaches for the past 3 months. The patient describes constant "dull pressure" in her head that is worse at the end of the day. She is an office manager and is able to work through the pain. The patient has a history of seasonal allergies and her sister has migraine headaches. Which of the following is the most likely diagnosis?

A. Chronic sinusitis
B. Cluster headache
C. Giant cell arteritis
D. Intracranial neoplasm
E. Migraine without aura
F. Tension headache

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A 27-year-old woman comes to the office due to almost daily headaches for the past 3 months. The patient describes constant "dull pressure" in her head that is worse at the end of the day. She is an office manager and is able to work through the pain. The patient has a history of seasonal allergies and her sister has migraine headaches. Which of the following is the most likely diagnosis?

A. Chronic sinusitis (16%)
B. Cluster headache (3%)
C. Giant cell arteritis (0%)
D. Intracranial neoplasm (2%)
E. Migraine without aura (4%)
✓ F. Tension headache (73%)

Correct

73%
Answered correctly

01 min, 02 secs
Time Spent

03/08/2021
Last Updated



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| | Types of headache | | |
|---|---|---|---|
| | **Migraine** | **Cluster** | **Tension** |
| **Sex predilection** | Female > male | Male > female | Female > male |
| **Family history** | Often present | ± | None |
| **Onset** | Variable | During sleep or similar timing daily | Under stress |
| **Location** | Often unilateral | Behind one eye | Band-like pattern around the head (bilateral) |
| **Character** | Pulsatile & throbbing | Excruciating, sharp & steady (ie, "ice-pick") | Dull, tight & persistent |
| **Duration** | 4-72 hours | 15-180 minutes | 30 minutes to months/years |
| | Photophobia | Ipsilateral sweating, facial | Muscle tenderness in |



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| | | | |
|---|---|---|---|
| **Associated symptoms** | Photophobia, phonophobia & nausea, ± aura | Ipsilateral sweating, facial flushing, nasal congestion, pupillary changes & lacrimation | Muscle tenderness in the head, neck, or shoulders |

This woman with dull, near-daily headaches has **tension headaches** (THs), the most common form of headache. THs are likely due to sensitization of peripheral nociceptors leading to increased perception of myofascial pain. Patients typically develop mild to moderate, achy, or pressure-like pain that is often **bilateral** and may involve the occipitonuchal, temporal, or frontal regions of the head. Pericranial **muscle tenderness** (eg, head, neck, shoulder) is common.

THs are not associated with other neurologic symptoms or nausea/vomiting and are often precipitated by **stress** and fatigue. They may persist for days, months, or even years but (unlike migraines and cluster headaches) do not typically limit a patient's ability to perform daily functions. Treatment is typically with **simple analgesics** (eg, nonsteroidal anti-inflammatory drugs, acetaminophen).

**(Choice A)** Chronic sinusitis can cause facial pain and tenderness but is often associated with nasal congestion and mucopurulent nasal drainage. A reduced sense of smell and taste is also common.

**(Choice B)** Cluster headaches most commonly affect men and present as severe, unilateral, orbital or temporal pain with associated autonomic symptoms (eg, lacrimation, rhinorrhea, diaphoresis). The


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temporal pain with associated autonomic symptoms (eg, lacrimation, rhinorrhea, diaphoresis). The headaches are typically brief (15-180 minutes), debilitating, and may awaken patients from sleep.

**(Choice C)** Giant cell arteritis is associated with an acute headache that is typically accompanied by scalp tenderness, visual symptoms, and jaw claudication. It occurs exclusively in older patients (age ≥50) and is often associated with polymyalgia rheumatica.

**(Choice D)** Brain tumors typically cause nausea, vomiting, and headaches that worsen with changes in body position. In addition, the presence of other focal neurologic signs would be expected due to compression of surrounding brain structures by the expanding tumor.

**(Choice E)** Migraine headaches are characterized by often debilitating, episodic, unilateral, pulsatile headaches typically associated with nausea, photophobia, and phonophobia. Some patients have focal neurologic symptoms that precede or accompany the headache (ie, aura).

**Educational objective:**
Tension headaches are the most common form of headache. They are characterized by an achy or pressure-like pain that is often bilateral and associated with pericranial muscle tenderness. Tension headaches are not associated with other neurologic symptoms and do not typically limit a patient's ability to perform daily functions.



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A 65-year-old man comes to the office due to tremors. He was diagnosed with idiopathic Parkinson disease 10 years ago and has since been successfully treated with levodopa/carbidopa. However, over the last several months, he has developed frequent "freezing" episodes characterized by a sudden loss of mobility. More recently, the patient's tremors worsened after he reduced his levodopa dose following the development of excessive body movements. On examination, he has a bilateral resting tremor that is worse on the right, bradykinesia, and cogwheel rigidity. He is interested in discussing surgical options. This patient would most likely benefit from high-frequency deep brain stimulation targeted at suppressing neuronal activity in which of the following brain structures?

A. Caudate nucleus
B. Globus pallidus externa
C. Putamen
D. Red nucleus
E. Subthalamic nucleus
F. Ventral intermediate nucleus of the thalamus



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last several months, he has developed frequent "freezing" episodes characterized by a sudden loss of mobility. More recently, the patient's tremors worsened after he reduced his levodopa dose following the development of excessive body movements. On examination, he has a bilateral resting tremor that is worse on the right, bradykinesia, and cogwheel rigidity. He is interested in discussing surgical options. This patient would most likely benefit from high-frequency deep brain stimulation targeted at suppressing neuronal activity in which of the following brain structures?

A. Caudate nucleus (11%)
B. Globus pallidus externa (28%)
C. Putamen (9%)
D. Red nucleus (2%)
E. Subthalamic nucleus (42%)
F. Ventral intermediate nucleus of the thalamus (4%)

Correct
42%
02 mins, 23 secs
10/03/2020


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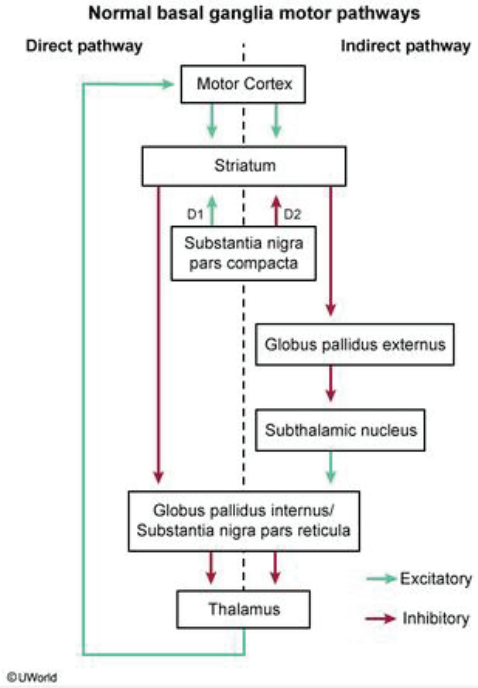


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This patient on long-term levodopa treatment for **Parkinson disease** has likely developed motor fluctuations and dyskinesia, which often occur >5 years after starting therapy. Motor fluctuations can initially correlate with serum drug levels and are characterized by good mobility during "on" periods and increased bradykinesia/rigidity during "off" periods when the drug wears off. Dyskinesia typically occurs when the patient is "on" and is characterized by excessive involuntary movements.

Nigrostriatal degeneration in Parkinson disease results in excessive excitation of the globus pallidus internus by the subthalamic nucleus, which in turn causes excessive inhibition of the thalamus. Reduced activity of the thalamus and its projections to the cortex consequently result in rigidity and bradykinesia. Patients with **medically intractable** symptoms of Parkinson disease may benefit from high-frequency deep brain stimulation of the globus pallidus internus or **subthalamic nucleus**. High-frequency stimulation **inhibits firing** of these nuclei. This causes increased activity in the downstream nuclei, resulting in **thalamo-cortical disinhibition** with improved mobility.

**(Choices A, B, C, and D)** These neural structures are not generally subjected to therapeutic high-frequency deep brain stimulation.

**(Choice F)** High-frequency stimulation of the ventral intermediate nucleus of the thalamus may reduce thalamic excitation and lessen excessive movements in patients with medically intractable essential tremor



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brain stimulation of the globus pallidus internus or **subthalamic nucleus**. High-frequency stimulation **inhibits firing** of these nuclei. This causes increased activity in the downstream nuclei, resulting in **thalamo-cortical disinhibition** with improved mobility.

**(Choices A, B, C, and D)** These neural structures are not generally subjected to therapeutic high-frequency deep brain stimulation.

**(Choice F)** High-frequency stimulation of the ventral intermediate nucleus of the thalamus may reduce thalamic excitation and lessen excessive movements in patients with medically intractable essential tremor.

**Educational objective:**

Nigrostriatal degeneration in Parkinson disease reduces activity of the thalamus and its projections to the cortex, resulting in bradykinesia and rigidity. Patients with medically intractable symptoms of Parkinson disease may benefit from high-frequency deep brain stimulation of the globus pallidus internus or subthalamic nucleus as it promotes thalamo-cortical disinhibition with improved mobility.

**References**


- Deep brain stimulation of the subthalamic nucleus in Parkinson's disease 2003-2013: Where are we another 10 years on?
- Deep brain stimulation for Parkinson disease: an expert consensus and review of key issues.




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A 22-year-old woman comes to the emergency department due to a severe left frontal headache for the past 30 minutes. The patient has had similar pain every day for the past 3 days, and the episodes resolve spontaneously after about an hour. She has no other medical conditions and takes no medications. On physical examination, the patient appears restless and in pain. There is ptosis on the left side. Which of the following findings is most suggestive of cluster headache in this patient?

- A. Episodic nature
- B. Female sex
- C. Frontal location
- D. Ipsilateral ptosis
- E. Unilateral pain

Submit



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A 22-year-old woman comes to the emergency department due to a severe left frontal headache for the past 30 minutes. The patient has had similar pain every day for the past 3 days, and the episodes resolve spontaneously after about an hour. She has no other medical conditions and takes no medications. On physical examination, the patient appears restless and in pain. There is ptosis on the left side. Which of the following findings is most suggestive of cluster headache in this patient?

A. Episodic nature (26%)
B. ~~Female sex~~ (1%)
C. Frontal location (5%)
D. Ipsilateral ptosis (49%)
E. ~~Unilateral pain~~ (16%)

Correct

49%
Answered correctly

01 min, 19 secs
Time Spent

12/13/2020
Last Updated



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| | Types of headache | | |
|---|---|---|---|
| | **Migraine** | **Cluster** | **Tension** |
| **Sex predilection** | Female > male | Male > female | Female > male |
| **Family history** | Often present | ± | None |
| **Onset** | Variable | During sleep or similar timing daily | Under stress |
| **Location** | Often unilateral | Behind one eye | Band-like pattern around the head (bilateral) |
| **Character** | Pulsatile & throbbing | Excruciating, sharp & steady (ie, "ice-pick") | Dull, tight & persistent |
| **Duration** | 4-72 hours | 15-180 minutes | 30 minutes to |


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| | | | |
|---|---|---|---|
| **Duration** | 4-72 hours | 15-180 minutes | months/years |
| **Associated symptoms** | Photophobia, phonophobia & nausea, ± aura | Ipsilateral sweating, facial flushing, nasal congestion, pupillary changes & lacrimation | Muscle tenderness in the head, neck, or shoulders |

This patient with recurrent, unilateral, severe headaches accompanied by ptosis has **cluster headache**, a type of trigeminal autonomic cephalalgia. Cluster headaches often present with rapid-onset, severe, unilateral pain that is typically periorbital, frontal, or temporal. Patients are often restless or agitated during episodes. Cluster headaches are often accompanied by **ipsilateral autonomic symptoms**, which may include:

- Conjunctival injection and lacrimation
- Nasal congestion or rhinorrhea
- **Ptosis**, miosis, and anhidrosis

Headaches typically last 15-180 minutes and tend to occur in clusters (up to 8 times daily, often at the same time of day) over a period of several weeks. In some patients, clusters occur at similar seasons of the year. This clustering may suggest involvement of the **hypothalamus**, which regulates circadian


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same time of day) over a period of several weeks. In some patients, clusters occur at similar seasons of the year. This clustering may suggest involvement of the **hypothalamus**, which regulates circadian rhythms. Treatment of acute headaches is often with oxygen or triptans (eg, sumatriptan); verapamil is frequently used for preventive treatment.

**(Choice A)** Both migraines and cluster headaches tend to have discrete episodes, so episodic nature is not a distinguishing feature in itself. The timing of the episodes (eg, around the same time every day, several days in a row) and the duration (eg, 15-180 min) are more characteristic of cluster headache, but the most obvious differentiating feature is the presence of autonomic symptoms.

**(Choice B)** Cluster headaches can occur in anyone, but they are more common in male patients.

**(Choice C)** Although cluster headaches are located in the frontal region, other types of headaches can also be frontal in location (eg, sinusitis, migraine), so this is not a specific differentiating feature.

**(Choice E)** Although cluster headaches are typically unilateral, migraine headaches are also often unilateral, so this is not helpful in distinguishing between those.

**Educational objective:**
Cluster headaches often present with rapid-onset, severe, unilateral pain accompanied by ipsilateral


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**(Choice A)** Both migraines and cluster headaches tend to have discrete episodes, so episodic nature is not a distinguishing feature in itself. The timing of the episodes (eg, around the same time every day, several days in a row) and the duration (eg, 15-180 min) are more characteristic of cluster headache, but the most obvious differentiating feature is the presence of autonomic symptoms.

**(Choice B)** Cluster headaches can occur in anyone, but they are more common in male patients.

**(Choice C)** Although cluster headaches are located in the frontal region, other types of headaches can also be frontal in location (eg, sinusitis, migraine), so this is not a specific differentiating feature.

**(Choice E)** Although cluster headaches are typically unilateral, migraine headaches are also often unilateral, so this is not helpful in distinguishing between those.

**Educational objective:**
Cluster headaches often present with rapid-onset, severe, unilateral pain accompanied by ipsilateral autonomic symptoms (eg, ptosis, miosis, nasal congestion, conjunctival injection).

| Pathology | Nervous System | Cluster headache |
|---|---|---|
| Subject | System | Topic |



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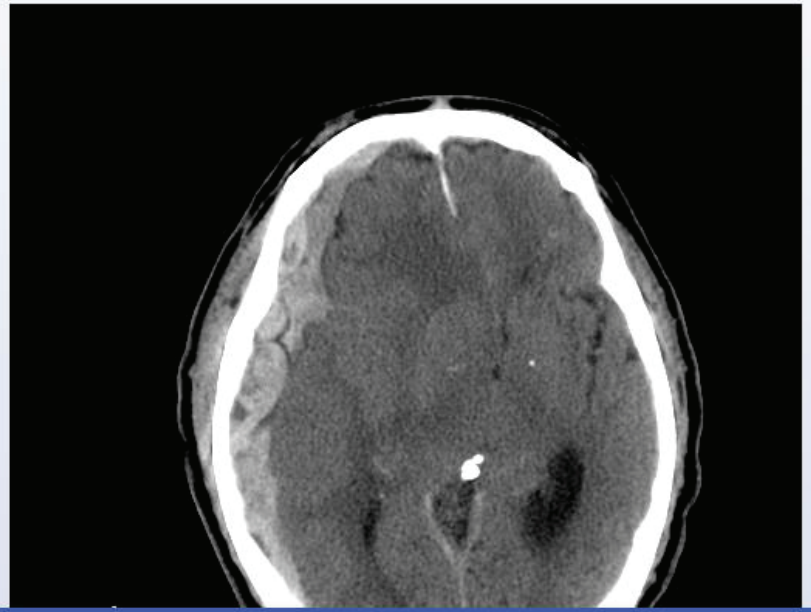
A 78-year-old female is brought to the ER because of altered mental status of recent onset and difficulty walking. She has a history of Parkinsonism and has had difficulty walking lately. She lives alone and has had a few falls recently. Her BP is 180/100 mm Hg and pulse is 68/min. Her CT scan of the head is shown below.





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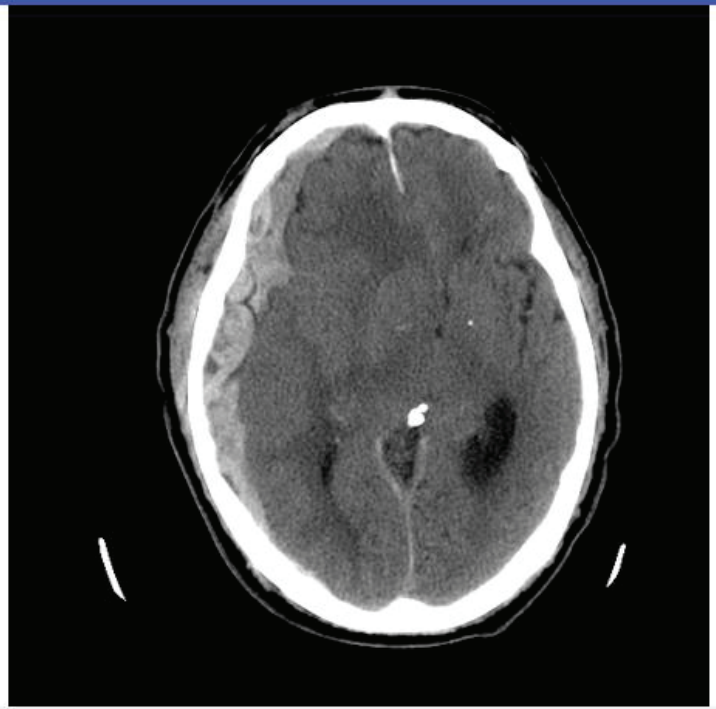

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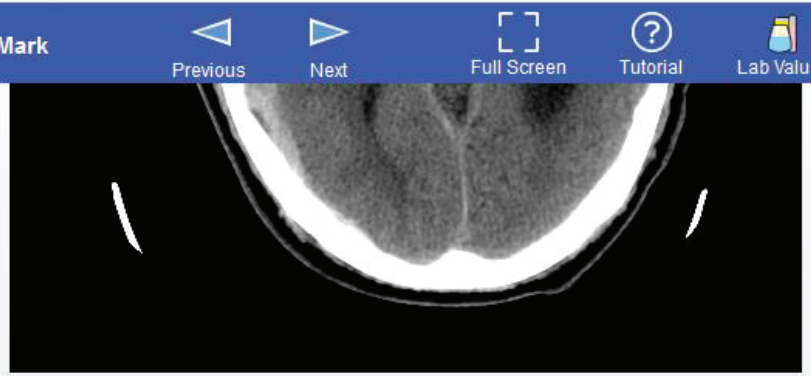

Which of the following is the most likely cause of her symptoms?

A. Rupture of middle meningeal artery
B. Rupture of cortical bridging veins
C. Rupture of lateral striate arteries
D. Rupture of berry aneurysm
E. Rupture of posterior communicating artery

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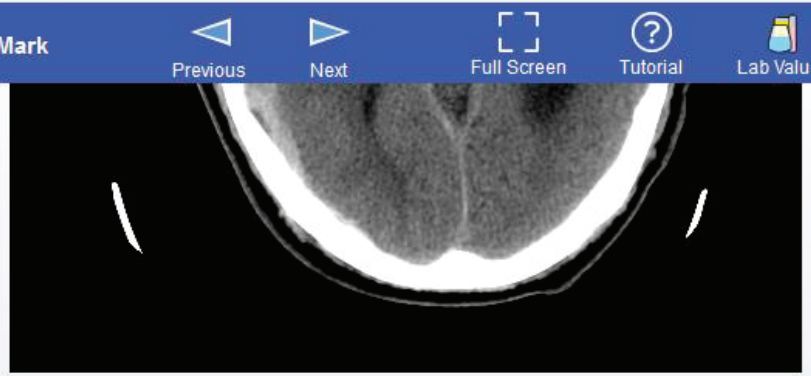

Which of the following is the most likely cause of her symptoms?

A. Rupture of middle meningeal artery (16%)

B. Rupture of cortical bridging veins (76%)

C. Rupture of lateral striate arteries (2%)

D. ~~Rupture of berry aneurysm~~ (2%)

E. ~~Rupture of posterior communicating artery~~ (1%)

Correct

76%

01 min, 21 secs

12/09/2020



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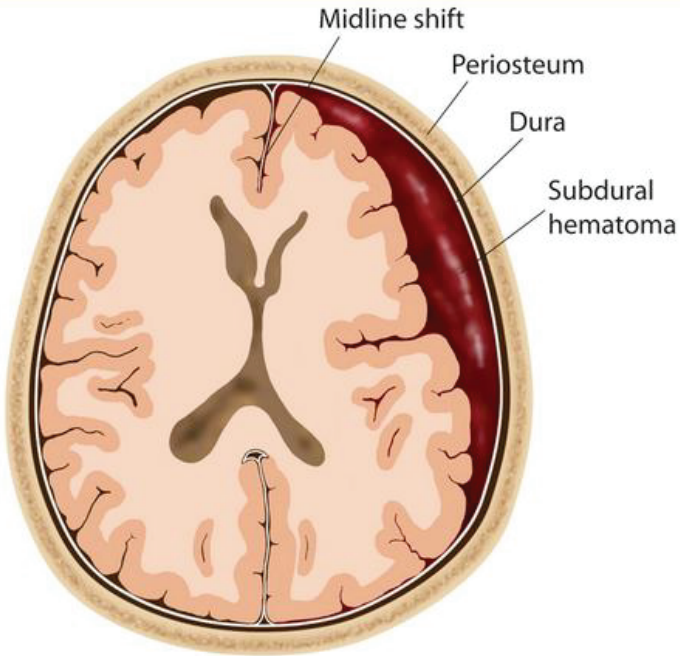


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This patient has suffered a subdural hematoma, an accumulation of blood between the dura mater and arachnoid. The blood comes from the bridging cortical veins which carry blood from the cortex to the venous sinuses. They can rupture as a result of acceleration-deceleration injury. As the hematoma expands, it raises the intracranial pressure and compresses the brain. Venous bleeding is relatively slow, which explains the **gradual onset of symptoms** in subdural hematoma. Patients complain of gradually worsening headache and display a slow decline in mental function. On CT scan, subdural hematoma is seen as a **crescent-shaped** mass.

Subdural hematoma often occurs in elderly individuals after a minor trauma. This increased incidence is explained by age-related brain atrophy. As the distance from the skull to the brain surface increases, cortical bridging veins are under more tension and rupture more easily. In elderly patients, subdural bleeding is called a "great imitator" due to its subtle and variable presentation. It may present as gait abnormalities, seizures, somnolence, confusion and memory loss. These patients may go undiagnosed for weeks.

**(Choice A)** Rupture of the middle meningeal artery causes epidural hemorrhage. Its clinical presentation is characterized by a "lucid interval", followed by loss of consciousness. A biconvex hematoma is seen on CT scan.



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**(Choice C)** The lateral striate arteries arise from the middle cerebral arteries. They are also called the penetrating branches. These vessels supply the internal capsule and the basal ganglia, and often rupture in hypertensive strokes.

**(Choices D and E)** The posterior communicating artery is the second most common site of rupture of berry aneurysms in the circle of Willis (anterior communicating artery is the most common site). This results in subarachnoid bleeding. It manifests with a severe headache that may be described as "the worst headache of my life". Fever and nuchal rigidity are commonly present.

**Educational objective:**
Subdural hematoma occurs due to the rupture of cortical bridging veins. In young patients, it results from a fall or motor vehicle accident, and manifests with gradual onset of headache and confusion. In elderly patients it may occur after a minor trauma and present with a variety of neurologic symptoms. You should know how to recognize this on CT scan.

| Pathology | Nervous System | Subdural hematoma |
|---|---|---|
| Subject | System | Topic |

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A 55-year-old man with HIV comes to the emergency department due to 3 weeks of increasing headache, fever, and vomiting. Examination shows low blood pressure and neck stiffness. The patient's condition quickly deteriorates, and he dies in the hospital despite appropriate treatment. Autopsy of the brain shows a diffuse gelatinous exudate covering the base of the brain. Cut sections of the brain show marked ventriculomegaly and frontal lobe infarcts but no intraparenchymal mass lesions. Which of the following is the most likely diagnosis?

A. Herpes simplex infection
B. Neurocysticercosis
C. Primary CNS lymphoma
D. Toxoplasmosis
E. Tuberculosis infection

Submit



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A 55-year-old man with HIV comes to the emergency department due to 3 weeks of increasing headache, fever, and vomiting. Examination shows low blood pressure and neck stiffness. The patient's condition quickly deteriorates, and he dies in the hospital despite appropriate treatment. Autopsy of the brain shows a diffuse gelatinous exudate covering the base of the brain. Cut sections of the brain show marked ventriculomegaly and frontal lobe infarcts but no intraparenchymal mass lesions. Which of the following is the most likely diagnosis?

A. Herpes simplex infection (21%)
B. Neurocysticercosis (14%)
C. Primary CNS lymphoma (15%)
D. Toxoplasmosis (12%)
✓ E. Tuberculosis infection (35%)

Correct

35% Answered correctly
40 secs Time Spent
01/05/2021 Last Updated



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This patient's subacute symptoms and autopsy findings are highly suggestive of **tuberculous (TB) meningitis**, the most common central nervous system (CNS) manifestation of disseminated TB. TB meningitis arises when circulating bacilli lodge in the subependymal or subpial space, forming a tubercle that subsequently ruptures into the subarachnoid space. Common findings include the following:

- A **thick, gelatinous exudate** most prominent in the **basal portion of the brain**. This exudate can encase the cranial nerves, leading to cranial nerve palsy, and invade the circle of Willis, leading to stroke.
- Tuberculous **vasculitis** of the cerebral arteries. This can cause **multiple bilateral brain infarctions**, particularly in the periventricular cerebral areas.
- **Hydrocephalus** due to obstruction of cerebrospinal fluid outflow by tubercular proteins. This can cause elevated intracranial pressure (eg, headache, nausea, vomiting) and **ventriculomegaly**.

Although CNS invasion occurs in only ~5% of extrapulmonary TB, risk is increased in those with significant immunocompromise due to **HIV**, immunosuppressive medications, advanced age, or malnutrition.

**(Choice A)** Herpes simplex virus type 1 can spread via the trigeminal nerve (CN V) to the brain. Patients usually develop rapid-onset (not subacute) fever, headache, seizure, altered mental status, and neurologic deficits. Autopsy typically shows unilateral temporal lobe inflammation, not hydrocephalus or a gelatinous


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**(Choice A)** Herpes simplex virus type 1 can spread via the trigeminal nerve (CN V) to the brain. Patients usually develop rapid-onset (not subacute) fever, headache, seizure, altered mental status, and neurologic deficits. Autopsy typically shows unilateral temporal lobe inflammation, not hydrocephalus or a gelatinous exudate in the basal brain.

**(Choice B)** Neurocysticercosis is caused by the larval stage of the pork tapeworm *Taenia solium*. It is generally marked by intraparenchymal cysts at several stages of development. The lack of intraparenchymal lesions makes neurocysticercosis unlikely. In addition, patients generally present with seizures or focal neurologic deficits.

**(Choice C)** Primary CNS lymphoma is more common in patients with HIV but is usually marked by a single large mass in the parenchyma of the brain. The presence of a thick, gelatinous exudate and no intraparenchymal brain lesions would be atypical.

**(Choice D)** *Toxoplasma* encephalitis is common in patients with advanced HIV who are not on prophylaxis. Although it often presents with slowly progressive headache, vomiting, and/or fever, it is marked by multiple intraparenchymal lesions in the brain.

**Educational objective:**

Tuberculous (TB) meningitis is characterized by formation of a thick, gelatinous exudate in the base of the



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intraparenchymal lesions makes neurocysticercosis unlikely. In addition, patients generally present with seizures or focal neurologic deficits.

**(Choice C)** Primary CNS lymphoma is more common in patients with HIV but is usually marked by a single large mass in the parenchyma of the brain. The presence of a thick, gelatinous exudate and no intraparenchymal brain lesions would be atypical.

**(Choice D)** *Toxoplasma* encephalitis is common in patients with advanced HIV who are not on prophylaxis. Although it often presents with slowly progressive headache, vomiting, and/or fever, it is marked by multiple intraparenchymal lesions in the brain.

**Educational objective:**

Tuberculous (TB) meningitis is characterized by formation of a thick, gelatinous exudate in the base of the brain; cerebral vasculitis; and hydrocephalus. It frequently presents with subacute, slowly progressive nausea, vomiting, fever, cranial nerve deficits, and strokes.

**References**

- Fulminant tuberculous meningitis—autopsy case report.

Pathology Nervous System Tuberculosis


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A 54-year-old hospitalized man develops new-onset slurring of speech and extremity weakness. Medical history is significant for alcohol abuse. Physical examination reveals confusion, dysarthria, dysphagia, and quadriparesis. MRI of the brain shows symmetric areas of demyelination in the pons. Which of the following most likely predisposed this patient to his current condition?

A. Atheroma formation in the vertebrobasilar arteries
B. Hematogenous dissemination of microbial agents
C. Nutritional deficiency of water-soluble vitamin
D. Overly rapid correction of electrolyte abnormalities
E. Paraneoplastic production of anti-neuronal antibodies

Submit



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A 54-year-old hospitalized man develops new-onset slurring of speech and extremity weakness. Medical history is significant for alcohol abuse. Physical examination reveals confusion, dysarthria, dysphagia, and quadriparesis. MRI of the brain shows symmetric areas of demyelination in the pons. Which of the following most likely predisposed this patient to his current condition?

A. Atheroma formation in the vertebrobasilar arteries (1%)
B. Hematogenous dissemination of microbial agents (0%)
C. Nutritional deficiency of water-soluble vitamin (23%)
✓ D. Overly rapid correction of electrolyte abnormalities (74%)
E. Paraneoplastic production of anti-neuronal antibodies (0%)

Correct
74% Answered correctly
54 secs Time Spent
09/26/2020 Last Updated

Explanation



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Normonatremia

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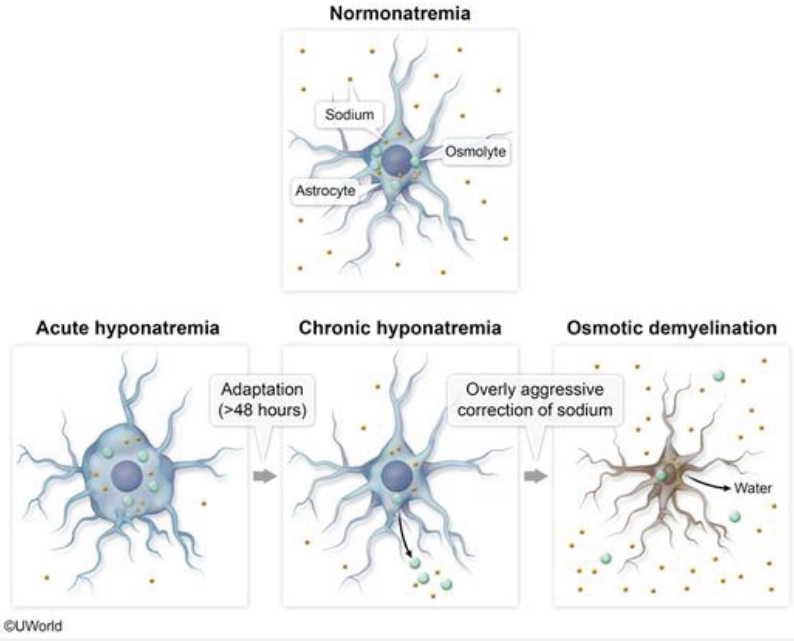
Osmotic demyelination syndrome

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This patient with a history of alcohol abuse has new-onset **pseudobulbar palsy** (dysarthria, dysphagia, dysphonia) and **quadriparesis** suggesting a brainstem insult. In association with the focal, symmetric **demyelination of the pons** noted on MRI, this presentation suggests **osmotic demyelination syndrome** (ODS), also known as central pontine myelinolysis. Other classic clinical features include a horizontal gaze paralysis, obtundation, and "locked in" syndrome, in which patients are aware but unable to move or communicate verbally.

Decreased plasma osmolality from hyponatremia (common in patients with alcohol abuse) results in water flowing across the osmotic gradient into brain cells; if this happens acutely, life-threatening cerebral edema can occur. However, with slowly developing (chronic) hyponatremia, astrocytes and oligodendrocytes excrete osmotically active organic solutes (eg, glutamate, myoinositol) to cause compensatory intracellular water loss and normalization of brain volume. Therefore, chronic hyponatremia can present with minimal neurologic symptoms.

However, **overly rapid correction of chronic hyponatremia** (eg, bolus of normal saline) reverses the osmotic gradient, drawing water from the cells into the plasma. The astrocytes and oligodendrocytes are unable to rapidly re-accumulate the lost organic solutes, resulting in cell shrinkage, dehydration, and apoptosis. The resultant demyelination preferentially affects the pons, possibly because the cells there are



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apoptosis. The resultant demyelination preferentially affects the pons, possibly because the cells there are less metabolically active and less able to rapidly regenerate organic solutes.

**(Choice A)** Vertebrobasilar atheroma formation can result in a pontine stroke with similar symptoms; however, ischemia (not demyelination) is expected on MRI.

**(Choice B)** Septic emboli (hematogenous spread of bacteria or fungi) are typically associated with endocarditis. Symptomatic brain abscesses can occur (eg, headache, focal neurologic findings), but MRI would demonstrate ring enhancement with vasogenic edema.

**(Choice C)** The administration of glucose-containing fluids to patients with thiamine deficiency (common in patients with alcohol abuse) can cause Wernicke encephalopathy (ie, ataxia, oculomotor dysfunction, encephalopathy). Korsakoff syndrome (chronic memory impairment) can also occur. Mamillary body atrophy is often visible on MRI.

**(Choice E)** Paraneoplastic production of anti-neuronal antibodies can be seen in a variety of malignancies (eg, small cell lung cancer, thymoma), but symptoms are often nonfocal (eg, altered mentation, seizures). Demyelination is unexpected.

**Educational objective:**

Osmotic demyelination syndrome results from overly rapid correction of chronic hyponatremia. Clinical



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**(Choice C)** The administration of glucose-containing fluids to patients with thiamine deficiency (common in patients with alcohol abuse) can cause Wernicke encephalopathy (ie, ataxia, oculomotor dysfunction, encephalopathy). Korsakoff syndrome (chronic memory impairment) can also occur. Mamillary body atrophy is often visible on MRI.

**(Choice E)** Paraneoplastic production of anti-neuronal antibodies can be seen in a variety of malignancies (eg, small cell lung cancer, thymoma), but symptoms are often nonfocal (eg, altered mentation, seizures). Demyelination is unexpected.

**Educational objective:**
Osmotic demyelination syndrome results from overly rapid correction of chronic hyponatremia. Clinical features include quadriplegia, pseudobulbar palsy, and reduced level of consciousness. MRI demonstrates focal demyelination of the pons.

| Pathophysiology | Nervous System | Central pontine myelinolysis |
|---|---|---|
| Subject | System | Topic |

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A 30-year-old man comes to the emergency department with severe headache and neck pain following a motor vehicle collision. The patient has no blurry or double vision, dizziness, slurred speech, numbness, or weakness. Neuroimaging is unremarkable except for evidence of a right transverse foramina fracture at the level of C2. The patient is placed in a cervical collar and admitted for further evaluation. While in the hospital, he suddenly develops dizziness, right facial numbness, and hoarseness. Temperature is 36.7 C (98 F), blood pressure is 160/90 mm Hg, pulse is 80/min, and respirations are 12/min. Neurologic examination shows partial ptosis and miosis of the right eye, as well as nystagmus. Hearing is intact bilaterally. There is reduced sensation to pain and temperature on the right side of the face and the left side of the body. The patient is ataxic and displays past-pointing with his right hand on finger-to-nose testing. Vascular imaging will most likely reveal an acute dissection in which of the following arteries?

A. Basilar
B. Common carotid
C. Internal carotid
D. Middle cerebral
E. Posterior cerebral



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A. Basilar
B. Common carotid
C. Internal carotid
D. Middle cerebral
E. Posterior cerebral
F. Vertebral

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A. Basilar (17%)
B. ~~Common carotid~~ (1%)
C. ~~Internal carotid~~ (8%)
D. ~~Middle cerebral~~ (7%)
E. ~~Posterior cerebral~~ (14%)
F. Vertebral (49%)



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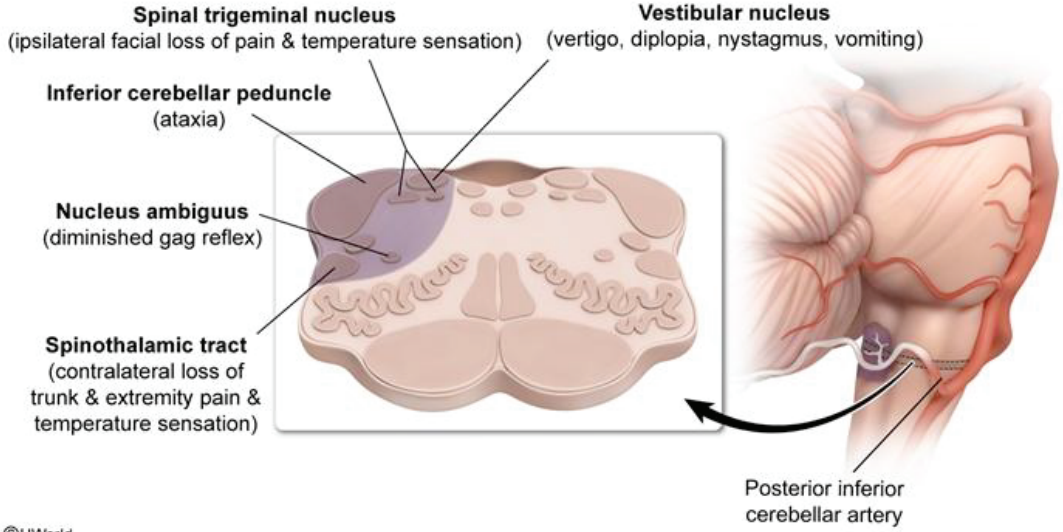
## Lateral medullary (Wallenberg) syndrome

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cerebellar artery

This patient's neurologic findings are consistent with acute ischemia involving the right **posterior inferior cerebellar artery** (PICA), which arises from the vertebral artery. Occlusion of the PICA results in **lateral medullary (Wallenberg) syndrome**. Characteristic features include vertigo/nystagmus, ipsilateral cerebellar signs (eg, ataxia), loss of pain/temperature sensation in the ipsilateral face and contralateral body, and bulbar weakness (eg, dysphagia, dysphonia). Patients may also develop ipsilateral Horner syndrome (ie, miosis, ptosis, anhidrosis) due to damage of sympathetic fibers innervating the head.

**Traumatic vascular dissection** is a relatively common cause of ischemic stroke in the young, with most cases affecting the extracranial vessels (eg, carotid and vertebral arteries). The vertebral arteries course through the transverse foramina in the neck before entering the skull at the foramen magnum and therefore can be easily injured by **cervical spinal trauma**. Progressive dissection can ascend intracranially to involve the section of the vertebral artery where the PICA branches off, leading to delayed development of lateral medullary syndrome (as in this patient with a normal initial examination).

**(Choice A)** Anterior inferior cerebellar artery (AICA) occlusion (ie, lateral pontine syndrome) due to basilar artery dissection could cause many of this patient's symptoms (eg, ataxia, nystagmus, vertigo, loss of facial sensation). However, traumatic dissection of the basilar artery is rare, and patients with AICA occlusion usually also have hearing loss and facial paralysis.



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cerebellar artery

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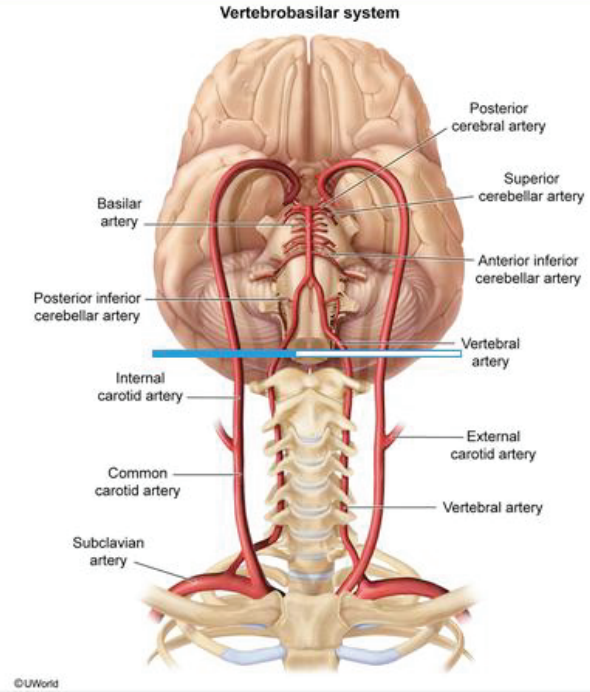


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usually also have hearing loss and facial paralysis.

**(Choices B and C)** Common and internal carotid artery dissections can occur with cervical spinal injuries. However, carotid artery occlusion typically causes profound neurologic deficits (eg, contralateral homonymous hemianopsia, hemiparesis, hemisensory loss) due to hemispheric cerebral infarction.

**(Choices D and E)** Traumatic dissections involving the intracranial arteries are rare. These vessels are typically occluded by atherothrombosis or cardioembolism in older adults with cardiovascular risk factors. Middle cerebral artery occlusion causes contralateral hemiparesis and hemisensory loss (face and arm > leg), conjugate gaze deviation, contralateral homonymous hemianopsia, and aphasia if the dominant (usually left) hemisphere is involved. Posterior cerebral artery occlusion causes contralateral, homonymous hemianopsia with macular sparing because the macula is also supplied by the middle cerebral artery.

**Educational objective:**
Cervical spine trauma can cause dissection of the vertebral artery, resulting in ischemic manifestations due to occlusion of the vertebral artery and/or its branches. Posterior inferior cerebellar artery occlusion causes lateral medullary (Wallenberg) syndrome, characterized by vertigo/nystagmus, ipsilateral cerebellar signs, loss of pain/temperature sensation in the ipsilateral face and contralateral body, bulbar weakness, and


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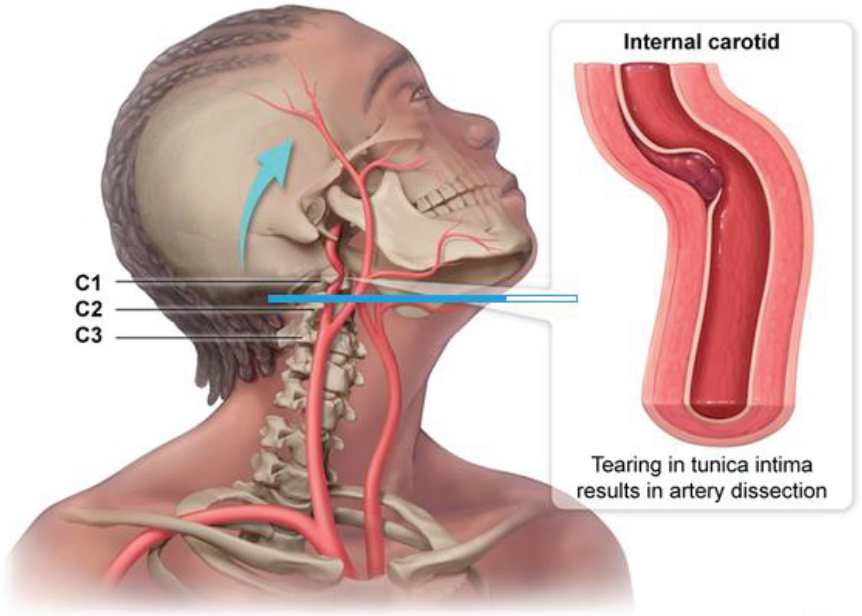
Neck manipulation (eg, trauma, sports, chiropractic manipulation)

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homonymous hemianopsia, hemiparesis, hemisensory loss) due to hemispheric cerebral infarction.

**(Choices D and E)** Traumatic dissections involving the intracranial arteries are rare. These vessels are typically occluded by atherothrombosis or cardioembolism in older adults with cardiovascular risk factors. Middle cerebral artery occlusion causes contralateral hemiparesis and hemisensory loss (face and arm > leg), conjugate gaze deviation, contralateral homonymous hemianopsia, and aphasia if the dominant (usually left) hemisphere is involved. Posterior cerebral artery occlusion causes contralateral, homonymous hemianopsia with macular sparing because the macula is also supplied by the middle cerebral artery.

**Educational objective:**

Cervical spine trauma can cause dissection of the vertebral artery, resulting in ischemic manifestations due to occlusion of the vertebral artery and/or its branches. Posterior inferior cerebellar artery occlusion causes lateral medullary (Wallenberg) syndrome, characterized by vertigo/nystagmus, ipsilateral cerebellar signs, loss of pain/temperature sensation in the ipsilateral face and contralateral body, bulbar weakness, and ipsilateral Horner syndrome.

**References**

- Extracranial carotid and vertebral artery dissection: a review.



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A medical research center is studying therapeutic options for the treatment of neuromuscular disorders. During experimentation, scientists develop a new drug that seems to have partial agonist/antagonist activity against receptor X. When the experimental drug is applied to cells expressing receptor X, there is an immediate change in transmembrane calcium, sodium, and potassium flow secondary to the opening of the receptor channel. Receptor X is most likely which type of receptor?

A. α1 adrenoreceptor
B. β1 adrenoreceptor
C. β2 adrenoreceptor
D. Muscarinic cholinergic receptor
E. Nicotinic cholinergic receptor

Submit



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A medical research center is studying therapeutic options for the treatment of neuromuscular disorders. During experimentation, scientists develop a new drug that seems to have partial agonist/antagonist activity against receptor X. When the experimental drug is applied to cells expressing receptor X, there is an immediate change in transmembrane calcium, sodium, and potassium flow secondary to the opening of the receptor channel. Receptor X is most likely which type of receptor?

A. α1 adrenoreceptor (5%)
B. β1 adrenoreceptor (13%)
C. β2 adrenoreceptor (3%)
D. Muscarinic cholinergic receptor (19%)
E. Nicotinic cholinergic receptor (57%)

Correct

57%
Answered correctly

02 mins, 14 secs
Time Spent

10/05/2020
Last Updated



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Cell membrane receptors can be divided into two broad categories: ionotropic receptors (ion channels that open directly upon ligand binding) and metabotropic receptors (these receptors utilize second messengers to indirectly influence their corresponding ion channels). Nicotinic cholinergic receptors of the neuromuscular junction are an example of a ligand-gated ion channel receptor (ionotropic receptor). As an action potential progresses to the presynaptic terminal, voltage-gated calcium channels open and allow entry of calcium into the nerve cytoplasm. This triggers the fusion of storage vesicles with the membrane, allowing a release of acetylcholine (ACh). This ACh diffuses across the synaptic cleft and ultimately interacts with nicotinic cholinergic receptors present on the motor end-plate. These receptors are ion channels that are comprised of five subunits with two ACh binding sites. If, and only if, both binding sites are filled, the ion channel will open. There is subsequent sodium and calcium **influx** and potassium **outflux** that results in the generation of an end-plate potential.

Nicotinic cholinergic receptors are also found in the CNS and on postganglionic neurons of autonomic ganglia. The description in the question stem most likely represents a nicotinic cholinergic receptor given the **immediate** flux of sodium, calcium, and potassium demonstrated by the scientists.

**(Choice A)** Binding of epinephrine to α1 adrenoceptors results in the activation of the inositol triphosphate



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ganglia. The description in the question stem most likely represents a nicotinic cholinergic receptor given the **immediate** flux of sodium, calcium, and potassium demonstrated by the scientists.

**(Choice A)** Binding of epinephrine to α1 adrenoceptors results in the activation of the inositol triphosphate ($IP_3$) pathway. This pathway results in increased intracellular calcium via release of $Ca^{2+}$ from storage organelles.

**(Choices B & C)** β1 and β2 adrenoceptors are associated with the cAMP signal transduction pathway. Stimulation of these receptors causes protein kinase A activation.

**(Choice D)** M1 and M3 muscarinic receptors utilize the inositol triphosphate pathway to increase intracellular calcium concentration and activate protein kinase C. M2 muscarinic receptors act via the cAMP second messenger system, and when activated decrease intracellular cAMP concentrations.

**Educational objective:**

The autonomic nervous system utilizes three types of signal pathways: cAMP, $IP_3$, and ion channels. Nicotinic receptors are ligand-gated ion channels that open after binding acetylcholine. This results in an immediate influx of $Na^+$ and $Ca^{2+}$ into the cell and an outflux of $K^+$ from the cell.

**References**

- Neuromuscular junction in health and disease.



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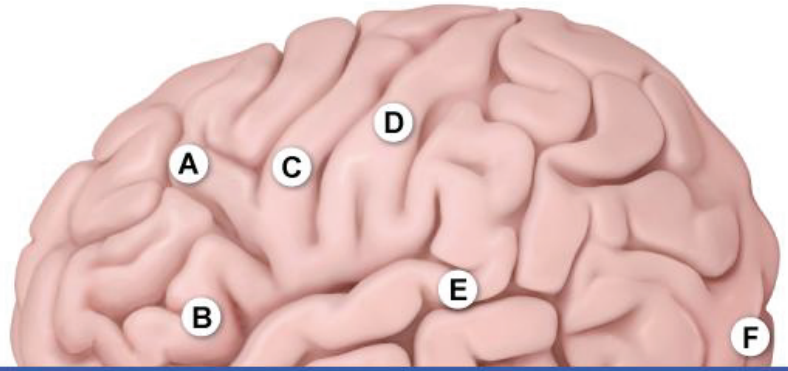
A 55-year-old right-handed man comes to the emergency department due to persistent right arm tingling and numbness for the past several hours. The patient has no headache, muscle weakness, slurred speech, or difficulty ambulating. He has a history of hypertension, paroxysmal atrial fibrillation, and ischemic stroke without residual symptoms. Anticoagulation was discontinued 2 months ago after he developed a gastrointestinal hemorrhage. Blood pressure is 150/90 mm Hg, and pulse is 92/min and regular. While the patient is being evaluated, his right arm paresthesia spreads to the entire right side of the body and he develops right-sided convulsions, followed by a bilateral tonic-clonic seizure. Which of the structures in the left cerebral hemisphere is the most likely site of origin of this patient's seizure?



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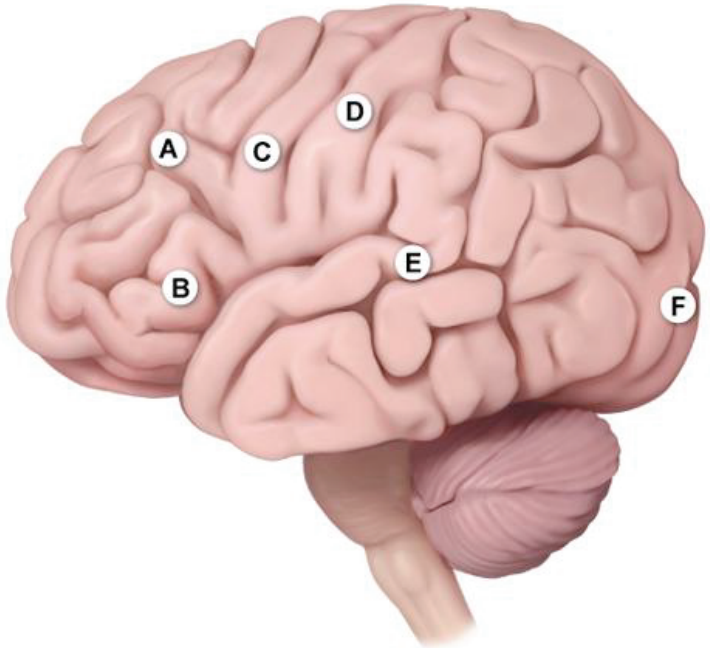


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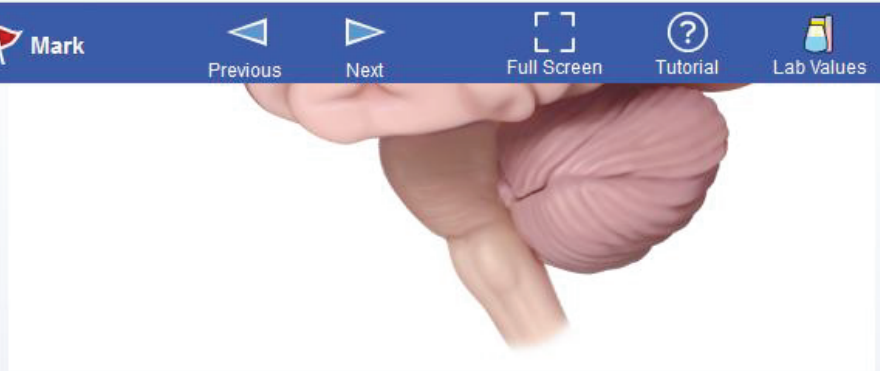

- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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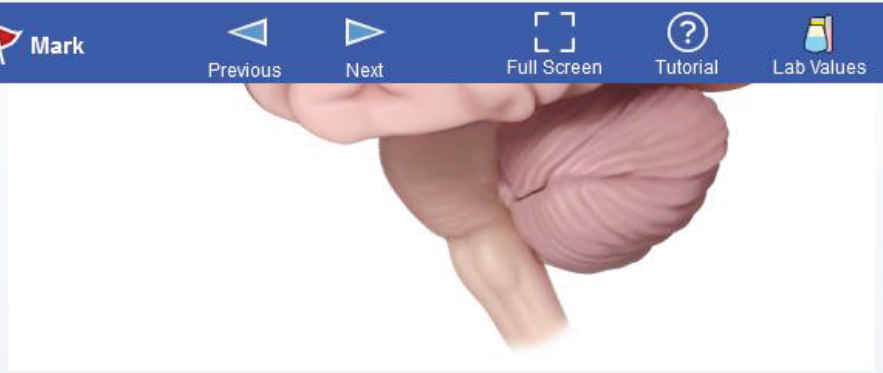

- A. A (2%)
- B. B (1%)
- C. C (27%)
- ✓ D. D (60%)
- E. E (7%)
- F. F (0%)

Correct

60%

01 min, 15 secs

11/27/2020



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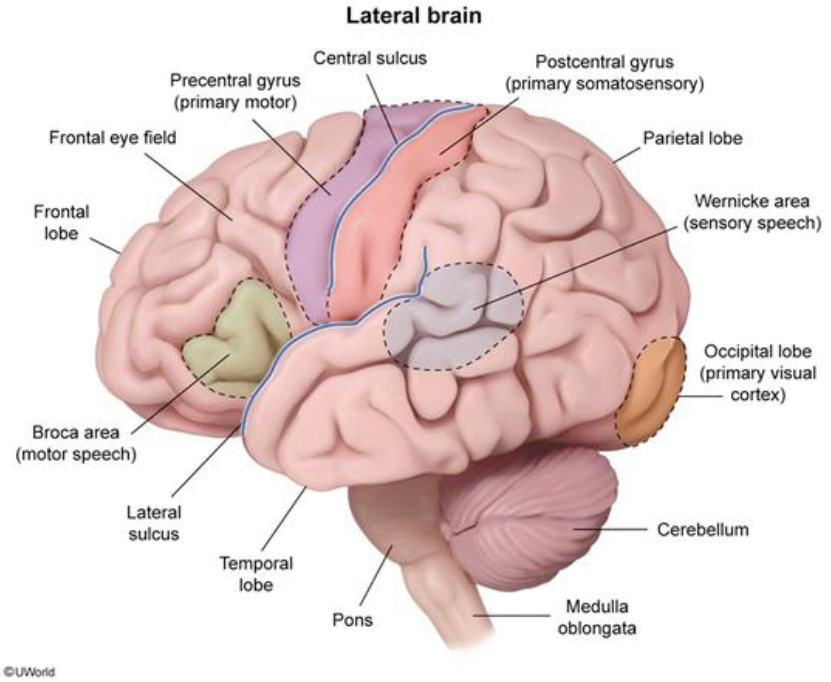


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This patient with a history of paroxysmal atrial fibrillation was taken off anticoagulation following a gastrointestinal bleed and is likely suffering from a recurrent **embolic stroke** complicated by seizure. Stroke is one of the most common causes of **seizure**, which occurs due to the release of excitotoxic neurotransmitters in the ischemic brain region.

Initial manifestations of a seizure vary based on which brain region is affected by the underlying pathology. The primary somatosensory cortex is responsible for processing all somatic sensory input from the contralateral side of the body; therefore, a seizure in this area of the cortex would result in contralateral sensory disturbances. This patient's **initial right arm numbness and paresthesia** was likely caused by a **focal onset seizure** originating in the left primary somatosensory cortex (**postcentral gyrus**).

The patient subsequently developed right-sided convulsions due to spread of the seizure along the lateral brain convexity to the primary motor strip (precentral gyrus) **(Choice C)**. Shortly after, the seizure activity spread to both cerebral hemispheres, resulting in tonic-clonic convulsions.

**(Choice A)** The frontal eye field is the region of the cerebral cortex that controls horizontal eye movement. Activation of the left frontal eye field during a seizure would cause the eyes to deviate horizontally to the right. After the seizure, the patient's eyes may temporarily deviate to the left due to postictal neuroinhibition



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neuroinhibition.

**(Choice B)** The motor speech (Broca) area is located in the posterior inferior frontal gyrus of the dominant (usually left) hemisphere and is responsible for controlling expressive speech/language. A seizure involving this area of the brain would likely result in uncontrolled vocalization or expressive aphasia.

**(Choice E)** The sensory speech (Wernicke) area is located in the posterior superior temporal gyrus of the dominant hemisphere and is responsible for language comprehension. A seizure in this area of the temporal lobe would likely result in fluent aphasia with impaired comprehension or auditory auras.

**(Choice F)** The primary visual cortex in the occipital lobe is responsible for processing visual information from the contralateral homonymous visual fields. A seizure originating from the left primary visual cortex would likely result in visual hallucinations affecting the right homonymous visual fields.

**Educational objective:**

The primary somatosensory cortex (postcentral gyrus) is responsible for processing all somatic sensory input from the contralateral side of the body. A focal onset seizure originating in this region of the cerebral cortex often results in contralateral sensory disturbance (eg, numbness, paresthesia).

**References**

- Symptoms in focal sensory seizures. Clinical and electroencephalographic features



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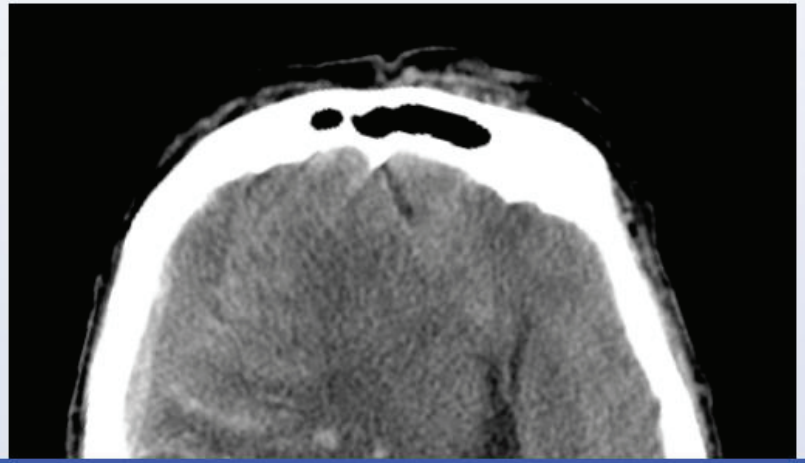
A 45-year-old man is brought to the emergency department after sustaining a traumatic head injury in a motor vehicle collision. The patient was found unresponsive and had several generalized tonic-clonic seizures during transport. Medical history includes hypertension as well as alcohol and cocaine misuse. Temperature is 36.7 C (98.1 F), blood pressure is 170/96 mm Hg, pulse is 50/min, and respirations are 10/min. Pulse oximetry shows 98% on mechanical ventilation with 50% oxygen. On examination, the patient is comatose with midpositioned and fixed pupils and rigid extension of the upper and lower extremities. Noncontrast CT scan of the head is shown in the image below:





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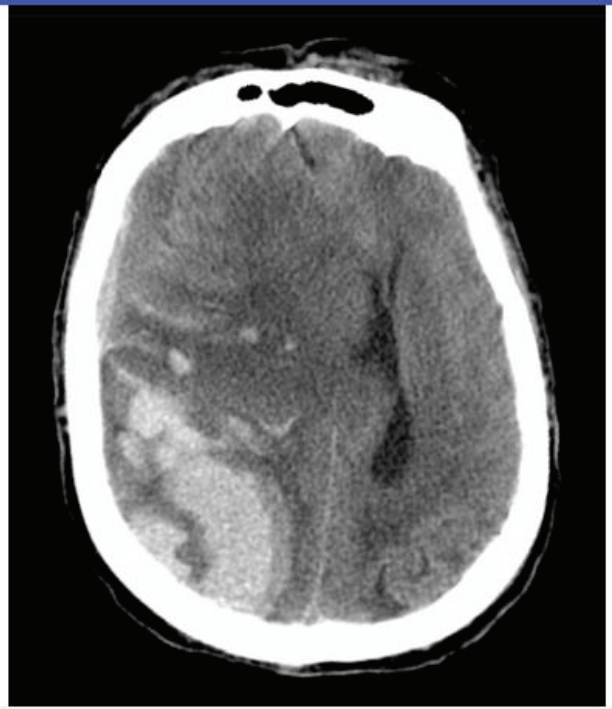

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Damage to which of the following structures is the most likely explanation for this patient's abnormal posturing?

- A. Cerebellar vermis
- B. Cerebral hemisphere
- C. Cervical spinal cord
- D. Internal capsule
- E. Pons
- F. Substantia nigra
- G. Thalamus

Submit



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Damage to which of the following structures is the most likely explanation for this patient's abnormal posturing?

- A. ~~Cerebellar vermis~~ (13%)
- B. ~~Cerebral hemisphere~~ (15%)
- C. ~~Cervical spinal cord~~ (4%)
- D. Internal capsule (12%)
- ✓ E. Pons (46%)
- F. Substantia nigra (3%)
- G. ~~Thalamus~~ (4%)

Correct

46%

01 min, 22 secs

11/04/2020



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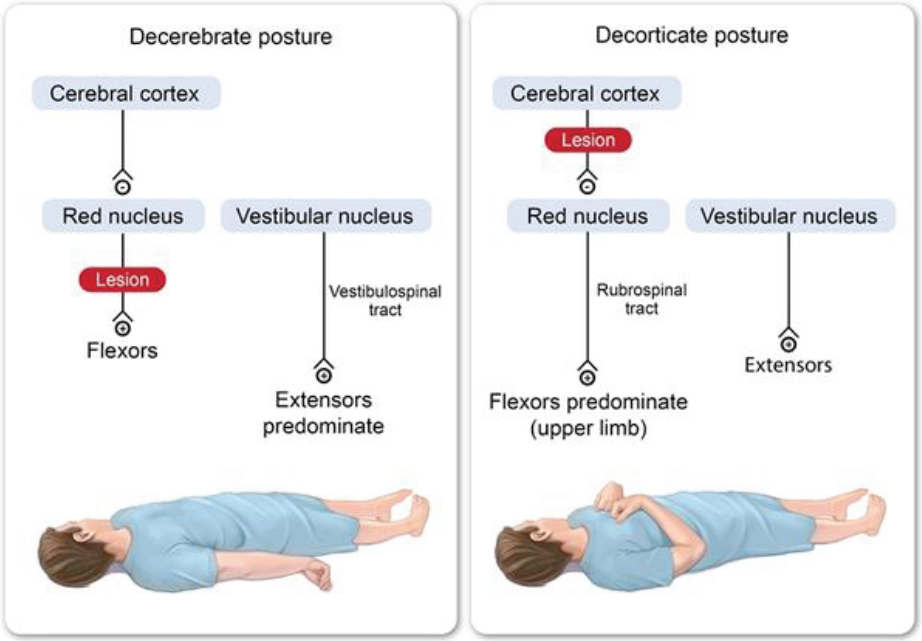
## Decerebrate vs decorticate posturing

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This patient who sustained a traumatic head injury has an extensive intraparenchymal hemorrhage that is likely complicated by brain herniation. Intracranial (eg, intraparenchymal) hemorrhage can cause significant mass effect and **increase intracranial pressure**, which can manifest with seizures and Cushing triad (hypertension, bradycardia, bradypnea). With further hemorrhagic expansion, horizontal shifts in midline structures or **brain herniation** may occur.

Progressive pupillary abnormalities are common in herniation. Uncal herniation initially disrupts the ipsilateral oculomotor nerve (CN III) leading to a **fixed dilated pupil**; however, as the brainstem becomes inferiorly displaced (ie, **central herniation**), damage to the midbrain and upper pons typically results in bilateral **midpositioned and fixed pupils** due to loss of both sympathetic and parasympathetic innervation.

Brain herniation also causes abnormal posturing from disruption of descending tracts (eg, rubrospinal, vestibulospinal) typically involved in reflexive and postural movements. The vestibulospinal tract maintains extensor tone and originates from vestibular nuclei at the pontomedullary junction. The **rubrospinal tract** regulates **upper extremity flexor** tone and originates from the red nuclei in the rostral midbrain; it is **inhibited by descending cortical input** from the cerebral cortex.



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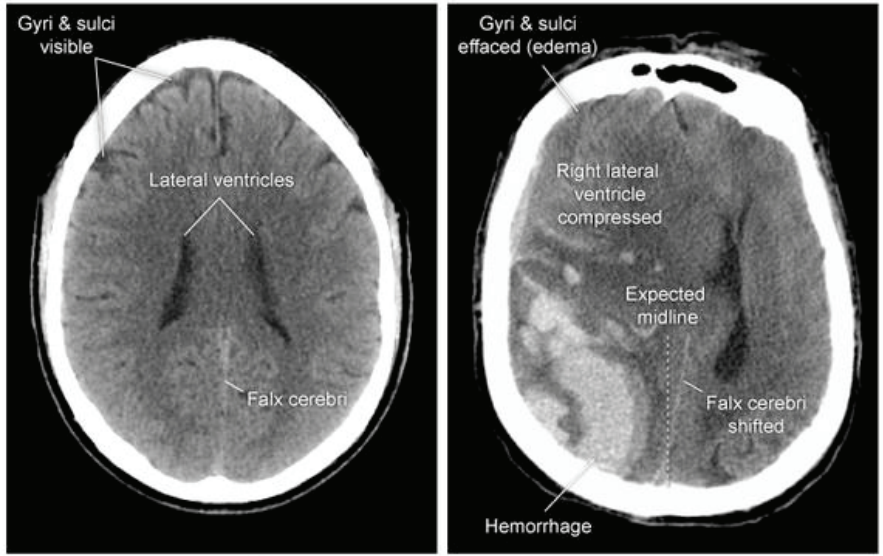
## Intraparenchymal brain hemorrhage




Normal head CT with symmetric cerebral hemispheres

Right cerebral intraparenchymal hemorrhage causing midline shift

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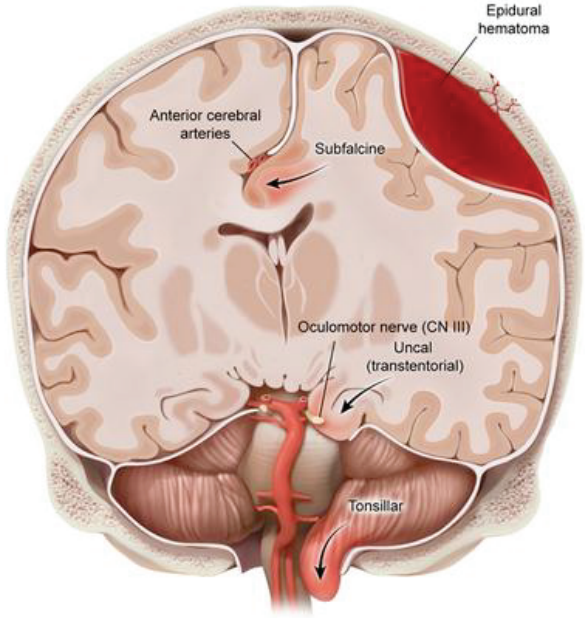
Types of brain herniation

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- **Damage above the red nucleus** (eg, cerebral hemisphere, internal capsule) typically results in **decorticate** (flexor) posturing due to loss of descending inhibition of the red nucleus and subsequent hyperactivity of upper limb flexors **(Choices B and D)**.
- **Damage below the red nucleus** (eg, **pons**) or to the nucleus itself (eg, midbrain) often causes **decerebrate** (extensor) posturing due to loss of descending excitation to the upper limb flexors (via the rubrospinal tract) and extensor predominance (due to unopposed vestibulospinal tract output).

**(Choice A)** Damage to the cerebellar vermis usually affects balance and coordination of the axial/proximal limb muscles, resulting in gait and truncal ataxia. Cerebellar vermis injury may also result in nystagmus and vertigo due to this structure's role in vestibular function.

**(Choice C)** The cervical spinal cord is commonly damaged in the setting of closed-head injury, which may lead acutely to flaccid quadriplegia/spinal shock (ie, absence of flexor and extensor motor tone) due to loss of excitatory input from the descending motor pathways.

**(Choice F)** Damage to the substantia nigra can result in excessive inhibition of the thalamus with subsequent decrease in excitation of the motor cortex. This leads to motor features of Parkinson disease (eg, rigidity, bradykinesia, tremor).


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of excitatory input from the descending motor pathways.

**(Choice F)** Damage to the substantia nigra can result in excessive inhibition of the thalamus with subsequent decrease in excitation of the motor cortex. This leads to motor features of Parkinson disease (eg, rigidity, bradykinesia, tremor).

**(Choice G)** The thalamus is a major relay station for motor and sensory information and also help regulate alertness and consciousness. Although bilateral damage to the thalamus may result in coma, flexor/extensor posturing is not characteristic of thalamic injury.

**Educational objective:**

Brain herniation causes abnormal posturing due to disruption of descending motor tracts (eg, rubrospinal, vestibulospinal). Damage above the level of the red nucleus (eg, cerebral hemispheres, internal capsule) typically results in decorticate (flexor) posturing. Damage at or below the red nucleus (eg, midbrain to pons) typically results in decerebrate (extensor) posturing.

**References**

- Neurological assessment of coma.

Pathology Nervous System Traumatic brain injury



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A 23-year-old, previously healthy man was involved in a motor vehicle collision. He lost consciousness at the scene but recovered by the time emergency medical services arrived. The patient was alert and awake in the ambulance but lost consciousness again soon after arriving at the emergency department. His breath smells of alcohol. Blood pressure is 130/90 mm Hg, pulse is 68/min, and respirations are 12/min. A bruise is noted over the left temple area. The left pupil is mildly dilated. Brain imaging would most likely reveal blood accumulating between which of the following tissues?

A. Aponeurosis and outer periosteum
B. Arachnoid mater and pia mater
C. Bone and dura mater
D. Dura mater and arachnoid mater
E. Pia mater and brain surface

Submit



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A 23-year-old, previously healthy man was involved in a motor vehicle collision. He lost consciousness at the scene but recovered by the time emergency medical services arrived. The patient was alert and awake in the ambulance but lost consciousness again soon after arriving at the emergency department. His breath smells of alcohol. Blood pressure is 130/90 mm Hg, pulse is 68/min, and respirations are 12/min. A bruise is noted over the left temple area. The left pupil is mildly dilated. Brain imaging would most likely reveal blood accumulating between which of the following tissues?

A. Aponeurosis and outer periosteum (1%)
B. Arachnoid mater and pia mater (5%)
C. Bone and dura mater (78%)
D. Dura mater and arachnoid mater (12%)
E. Pia mater and brain surface (2%)

Correct

78% Answered correctly

37 secs Time Spent

01/03/2021 Last Updated



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| Intracranial hemorrhage | | | |
|---|---|---|---|
| | **Epidural hematoma** | **Subdural hematoma** | **Subarachnoid hemorrhage** |
| **Vessel typically involved** | Middle meningeal artery | Bridging cortical veins | Aneurysm or arteriovenous malformation of anterior or posterior communicating arteries or MCA |
| **Location** | Between skull & dura mater | Between dura mater & arachnoid mater | Between arachnoid mater & pia mater |
| **Clinical manifestation** | Lucid interval, followed by loss of consciousness | Acute: coma at onset<br>Chronic: gradual onset of headache and confusion | Severe headache ("worst headache of my life"), nuchal rigidity |
| **Presentation on CT scan** | Biconvex hematoma | Crescent-shaped hematoma | Blood in the basal cisterns |

MCA= middle cerebral artery.


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MCA= middle cerebral artery.

Epidural hematoma is an accumulation of blood between the **skull bone and dura mater**. Most cases are due to fracture of the pterion region of the skull (often involving the temporal bone with associated scalp contusion) and a subsequent rupture or tear of the **middle meningeal artery**.

Epidural hematoma characteristically results in **transient loss of consciousness** at the time of impact followed by a **lucid period** in which the patient regains consciousness. However, the eventual expansion of the hematoma results in elevated intracranial pressure (ICP) and can lead to brain herniation, coma, and death. Signs of **elevated ICP** include altered mental status, nausea/vomiting, and Cushing reflex (ie, bradycardia, irregular breathing, hypertension). An **ipsilateral dilated pupil** can also occur due to uncal herniation and oculomotor nerve compression.

The diagnosis is confirmed with a noncontrast CT scan demonstrating a hyperdense, **biconvex** (lens-shaped) mass between the brain and skull. Epidural hematomas do not cross suture lines due to the tight adherence of the dura to the calvarium at these points.

**(Choice A)** The epicranial aponeurosis (galea aponeurotica) and outer periosteum cover the exterior surface of cranial bones. Intracranial hemorrhages are located inside the cranial vault.

**(Choice B)** Subarachnoid hemorrhage results in blood accumulation between the arachnoid mater and pia


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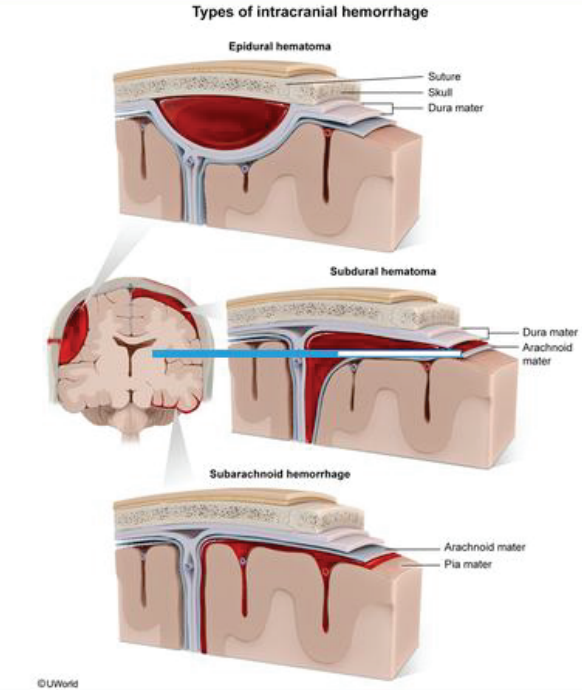


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(Choice B) Subarachnoid hemorrhage results in blood accumulation between the arachnoid mater and pia


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**(Choice B)** Subarachnoid hemorrhage results in blood accumulation between the arachnoid mater and pia mater. It most often occurs due to rupture of berry aneurysms or arteriovenous malformations of the anterior communicating, posterior communicating, or middle cerebral arteries. Patients typically have severe headache and nuchal rigidity.

**(Choice D)** Subdural hematoma (SDH) is located between the dura mater and arachnoid mater and results from tearing of the bridging cortical veins. It typically presents in older patients with profoundly depressed mental status at onset (acute SDH) or an insidious onset of headache and confusion (chronic SDH)

**(Choice E)** The pia mater is closely adherent to the brain surface and does not form a space for accumulation of blood.

**Educational objective:**
Epidural hematoma is an accumulation of blood between the bone and dura mater. It typically occurs due to a tear of the middle meningeal artery associated with fracture of the pterion region of the skull (often involving the temporal bone). Patients characteristically have transient loss of consciousness followed by a lucid interval before increasing intracranial pressure leads to neurologic deterioration.



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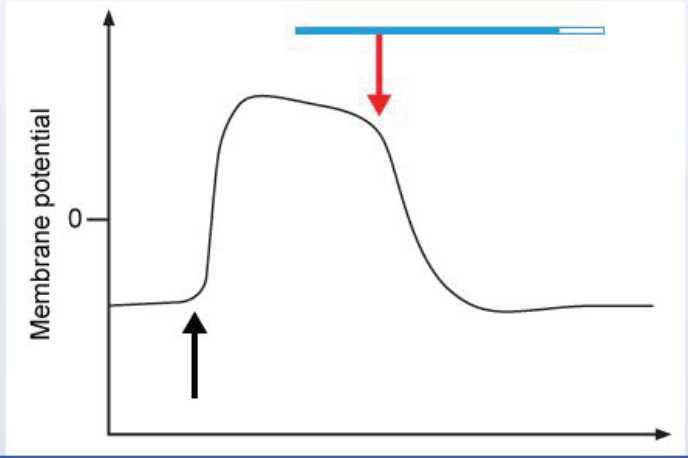
Researchers are studying how the membrane potential of a postsynaptic neuron changes in response to neurotransmitter stimulation. Baseline measurements determine that the resting membrane potential is generated by high membrane permeability for a particular ion. When neurotransmitter stimulation begins, ligand-gated ion channels open (black arrow) and increase the membrane permeability for a different ion, causing a change in membrane potential. This triggers the delayed opening of voltage-gated ion channels (red arrow), which increase the membrane permeability for a third type of ion. The results of the experiment are shown in the graph below.



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The equilibrium potentials of different ions under physiologic conditions are as follows:

$E_{Na} = +60$ mV

$E_{K} = -90$ mV

$E_{Cl} = -75$ mV

$E_{Ca} = +125$ mV

Which of the following options would best explain the changes in this neuron's membrane potential during the experiment?

| | Resting membrane permeability | Ligand-gated ion channel permeability | Voltage-gated ion channel permeability |
|---|---|---|---|
| A. | Sodium | Calcium | Chloride |
| B. | Sodium | Calcium | Potassium |
| C. | Potassium | Calcium | Sodium |



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$E_{Ca}$ = +125 mV

Which of the following options would best explain the changes in this neuron's membrane potential during the experiment?

| | Resting membrane permeability | Ligand-gated ion channel permeability | Voltage-gated ion channel permeability |
|---|---|---|---|
| A. | Sodium | Calcium | Chloride |
| B. | Sodium | Calcium | Potassium |
| C. | Potassium | Calcium | Sodium |
| D. | Potassium | Sodium | Calcium |
| E. | Potassium | Sodium | Chloride |

Submit



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$E_{Ca}$ = +125 mV

Which of the following options would best explain the changes in this neuron's membrane potential during the experiment?

| | Resting membrane permeability | Ligand-gated ion channel permeability | Voltage-gated ion channel permeability | |
|---|---|---|---|---|
| A. | ~~Sodium~~ | ~~Calcium~~ | ~~Chloride~~ | (2%) |
| B. | ~~Sodium~~ | ~~Calcium~~ | ~~Potassium~~ | (17%) |
| C. | ~~Potassium~~ | ~~Calcium~~ | ~~Sodium~~ | (15%) |
| D. | Potassium | Sodium | Calcium | (31%) |
| ✓ E. | Potassium | Sodium | Chloride | (32%) |

Correct

32%

02 mins, 48 secs

02/21/2021



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**Equilibrium potentials** of cellular ions reflect how they affect the membrane potential if the membrane were permeable solely for that ion. The resting membrane potential shown in the graph is negative, indicating that at rest, the membrane is permeable to an ion with a **negative equilibrium potential** (potassium or chloride). Opening of ligand-gated ion channels in response to neurotransmitter binding (black arrow) causes an increase in membrane potential to above zero. This indicates that the membrane has become permeable for an ion with a **positive equilibrium potential** (sodium or calcium). Opening of voltage-gated ion channels in response to the change in membrane potential (red arrow) causes a drop in membrane potential, indicating that the membrane becomes permeable to an ion with a **negative equilibrium potential** (potassium or chloride).

**(Choices A and B)** If the membrane were permeable for sodium at rest, the resting membrane potential would be positive as the equilibrium potential of sodium is +60 mV.

**(Choices C and D)** Had the membrane become more permeable for calcium or sodium following the opening of the voltage-gated ion channels, the membrane potential would have remained positive as both ions have positive equilibrium potentials.

**Educational objective:**

Changes in membrane potential occur in response to changes in neuronal membrane permeability to



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voltage-gated ion channels in response to the change in membrane potential (red arrow) causes a drop in membrane potential, indicating that the membrane becomes permeable to an ion with a **negative equilibrium potential** (potassium or chloride).

**(Choices A and B)** If the membrane were permeable for sodium at rest, the resting membrane potential would be positive as the equilibrium potential of sodium is +60 mV.

**(Choices C and D)** Had the membrane become more permeable for calcium or sodium following the opening of the voltage-gated ion channels, the membrane potential would have remained positive as both ions have positive equilibrium potentials.

**Educational objective:**
Changes in membrane potential occur in response to changes in neuronal membrane permeability to various cellular ions. The more permeable the membrane becomes for a cellular ion, the more that ion's equilibrium potential contributes to the total membrane potential.

| Physiology | Nervous System | Resting membrane potential and action potential |
|---|---|---|
| Subject | System | Topic |

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A 23-year-old woman has an acute attack of optic neuritis. She has a history of relapsing-remitting multiple sclerosis. An MRI of her brain reveals an area of demyelination involving the right optic nerve. Which of the following is most likely to be found on examination of both eyes?

| | Light in the right eye | | Light in the left eye | |
|---|---|---|---|---|
| | **Right pupil constriction** | **Left pupil constriction** | **Right pupil constriction** | **Left pupil constriction** |
| A. | Absent | Absent | Normal | Normal |
| B. | Absent | Normal | Absent | Normal |
| C. | Absent | Normal | Normal | Absent |
| D. | Normal | Absent | Normal | Absent |
| E. | Normal | Normal | Absent | Absent |

Submit



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A 23-year-old woman has an acute attack of optic neuritis. She has a history of relapsing-remitting multiple sclerosis. An MRI of her brain reveals an area of demyelination involving the right optic nerve. Which of the following is most likely to be found on examination of both eyes?

| | Light in the right eye | | Light in the left eye | | |
|---|---|---|---|---|---|
| | Right pupil constriction | Left pupil constriction | Right pupil constriction | Left pupil constriction | |
| ✓ A. | Absent | Absent | Normal | Normal | (75%) |
| B. | ~~Absent~~ | ~~Normal~~ | ~~Absent~~ | ~~Normal~~ | (16%) |
| C. | ~~Absent~~ | ~~Normal~~ | ~~Normal~~ | ~~Absent~~ | (3%) |
| D. | ~~Normal~~ | ~~Absent~~ | ~~Normal~~ | ~~Absent~~ | (2%) |
| E. | ~~Normal~~ | ~~Normal~~ | ~~Absent~~ | ~~Absent~~ | (2%) |

Correct

75%

01 min, 14 secs

09/19/2020



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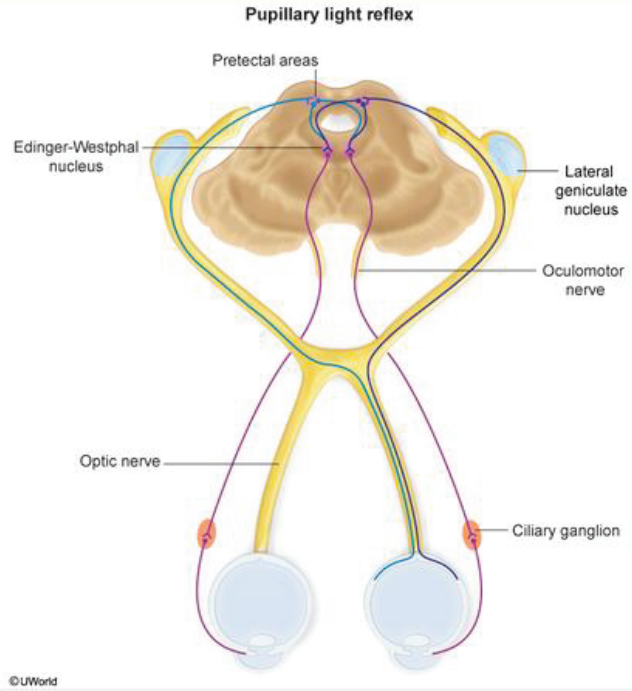


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This patient with unilateral optic neuritis is most likely to demonstrate an **afferent pupillary defect** due to **demyelination** of the right optic nerve (CNII). The **optic nerve** carries the afferent limb of the pupillary light reflex, transmitting information about light entering the eye to the pretectal area in the midbrain. The pretectal area activates the Edinger-Westphal nuclei bilaterally which send parasympathetic efferent (motor) fibers down the oculomotor nerve (CN III) to innervate the pupillary sphincter muscle of each iris. The crossovers in this pathway allow light entering one eye to cause both direct pupillary constriction in the ipsilateral eye and consensual pupillary constriction in the contralateral eye.

Patients with an afferent pupillary defect (eg, optic neuritis, retinal detachment) have sluggish or **absent bilateral pupillary constriction** when shining a **light into the affected eye** (in this case, a right afferent pupillary defect). However, signals from the eye on the unaffected side (the left eye in this patient) bypass the damaged optic nerve, resulting in normal pupillary constriction of both eyes **(Choice E)**.

**(Choices B and D)** An absent pupillary response in one eye when light enters either eye could occur with a defect in the efferent portion of the pupillary light reflex pathway carried by the oculomotor nerve (CNIII). Pupillary constriction in the eye ipsilateral to the lesion is impaired when light is shone in either eye; however, pupillary constriction in the contralateral eye occurs normally due to preserved afferent input bilaterally.


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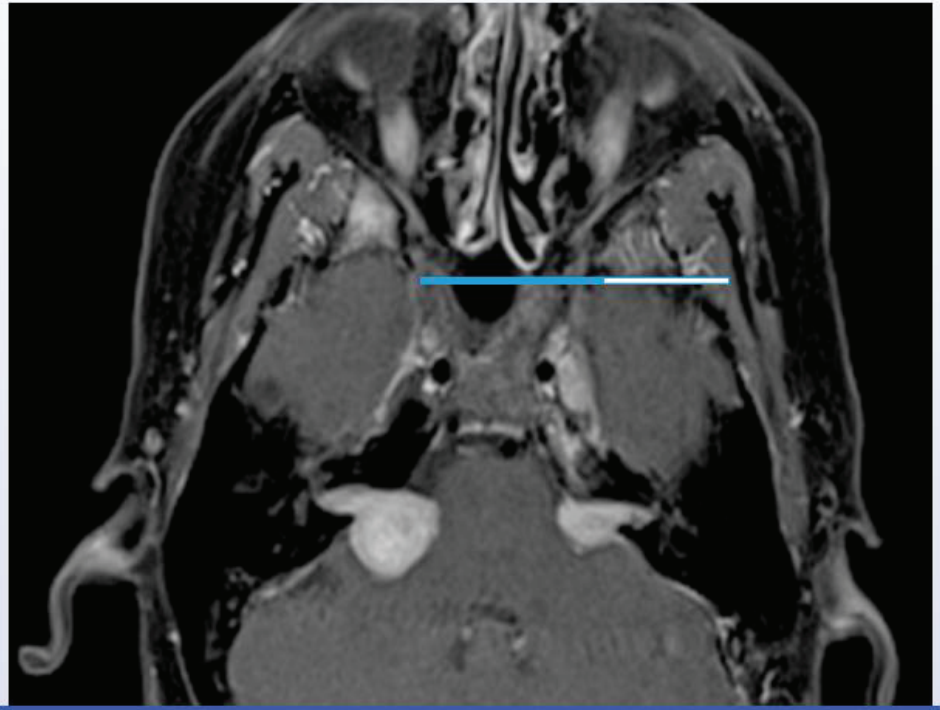
A 24-year-old man comes to the physician with complaints of tinnitus, vertigo, and hearing loss. A contrast-enhanced, T1-weighted image of his brain is shown below.





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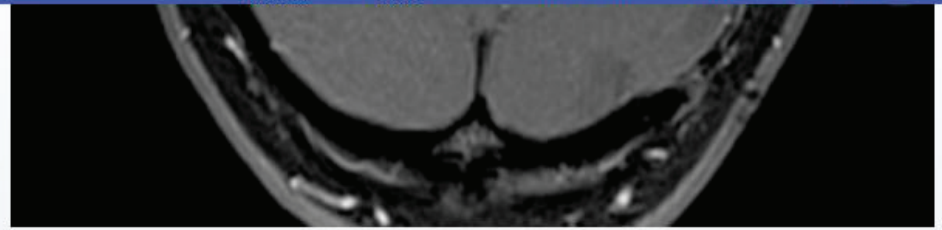

This patient's condition is most likely associated with a mutation involving which of the following genes?

A. APC on chromosome 5
B. NF1 on chromosome 17
C. NF2 on chromosome 22
D. p53 on chromosome 17
E. RB1 on chromosome 13
F. VHL on chromosome 3

Submit



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This patient's condition is most likely associated with a mutation involving which of the following genes?

- A. APC on chromosome 5 (0%)
- B. NF1 on chromosome 17 (8%)
- ✓ C. NF2 on chromosome 22 (84%)
- D. p53 on chromosome 17 (1%)
- E. RB1 on chromosome 13 (1%)
- F. VHL on chromosome 3 (3%)

Correct

84%

24 secs

10/21/2020



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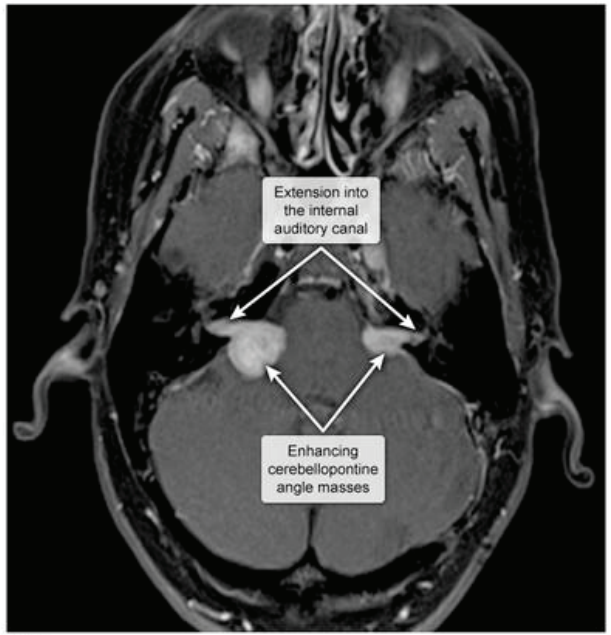
Acoustic neuromas

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The MRI image above shows bilateral tumors at the cerebellopontine angle. Most intracranial schwannomas are found at the cerebellopontine angle and are attached to CN VIII. Schwannomas at this location are called acoustic neuromas. Tinnitus, vertigo, and hearing loss are the typical symptoms of an acoustic neuroma. Bilateral acoustic neuromas occur in neurofibromatosis (NF) type 2. NF-2 differs from NF-1 in that it causes fewer cutaneous manifestations and presents with central nervous system involvement.

Both types of neurofibromatosis are **autosomal dominant** conditions, although they occur due to mutations on different chromosomes. The difference between these 2 diseases is summarized below.

| **Neurofibromatosis types 1 & 2** | | |
|---|---|---|
| **Diagnosis** | NF1 (von Recklinghausen disease) | NF2 (central neurofibromatosis) |
| **Gene mutation** | *NF1* tumor suppressor gene; codes the protein **neurofibromin** | *NF2* tumor suppressor gene; codes the protein **merlin** |
| **Location of mutated gene** | Chromosome 17 | Chromosome 22 |
| **Main clinical** | • Café-au-lait spots | |


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| | | |
|---|---|---|
| **Main clinical features** | • Café-au-lait spots<br>• Multiple neurofibromas<br>• Lisch nodules | • Bilateral acoustic neuromas |

**(Choice A)** Mutation of the APC gene (adenomatous polyposis coli) on chromosome 5 is associated with familial adenomatous polyposis syndromes and colon cancer.

**(Choice B)** Mutation of the NF-1 gene on chromosome 17 leads to NF-1. It is characterized by café-au-lait spots, Lisch nodules, and multiple neurofibromas. Bilateral acoustic neuromas are not characteristic of NF-1.

**(Choice D)** Mutation of p53 (the tumor suppressor gene on chromosome 17) is the most common mutation found in human cancers. It is also associated with Li-Fraumeni syndrome, a rare familial syndrome characterized by the development of breast cancer, sarcomas, brain tumors, leukemia, and adrenocortical tumors at a young age.

**(Choice E)** Mutation of the RB1 tumor suppressor gene on chromosome 13 increases the risk of retinoblastoma and osteosarcoma.

**(Choice F)** Mutation of the VHL gene on chromosome 3 occurs in von Hippel-Lindau disease. It is characterized by renal cysts, renal cell carcinomas, and hemangioblastomas of the cerebellum and retina.



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**(Choice D)** Mutation of p53 (the tumor suppressor gene on chromosome 17) is the most common mutation found in human cancers. It is also associated with Li-Fraumeni syndrome, a rare familial syndrome characterized by the development of breast cancer, sarcomas, brain tumors, leukemia, and adrenocortical tumors at a young age.

**(Choice E)** Mutation of the RB1 tumor suppressor gene on chromosome 13 increases the risk of retinoblastoma and osteosarcoma.

**(Choice F)** Mutation of the VHL gene on chromosome 3 occurs in von Hippel-Lindau disease. It is characterized by renal cysts, renal cell carcinomas, and hemangioblastomas of the cerebellum and retina.

**Educational objective:**
Bilateral acoustic neuromas are associated with neurofibromatosis type 2, an autosomal dominant condition caused by mutation of the NF-2 gene on chromosome 22.

| Pathology | Nervous System | Neurofibromatosis |
|---|---|---|
| Subject | System | Topic |

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A 3-year-old boy is brought to the office for follow-up on intellectual disability and speech delay. Review of his developmental screening questionnaire shows that the boy does not imitate his parents' activities, have a social smile, or show interest in other children. The patient has 8-10 words in his vocabulary and does not combine them into 2-word phrases. There is also concern that his verbal comprehension is poor, and a subsequent audiological evaluation was normal. The boy is up to date on all vaccinations and has no other significant medical history. Laboratory testing shows 226 CGG trinucleotide repeats in a gene located on the X chromosome. Which of the following is the most likely cause of this patient's clinical condition?

A. Exon deletion
B. Gene methylation
C. Impaired intron splicing
D. Imprinting
E. Mismatch repair defect

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A 3-year-old boy is brought to the office for follow-up on intellectual disability and speech delay. Review of his developmental screening questionnaire shows that the boy does not imitate his parents' activities, have a social smile, or show interest in other children. The patient has 8-10 words in his vocabulary and does not combine them into 2-word phrases. There is also concern that his verbal comprehension is poor, and a subsequent audiological evaluation was normal. The boy is up to date on all vaccinations and has no other significant medical history. Laboratory testing shows 226 CGG trinucleotide repeats in a gene located on the X chromosome. Which of the following is the most likely cause of this patient's clinical condition?

A. Exon deletion (8%)
B. Gene methylation (45%)
C. Impaired intron splicing (28%)
D. Imprinting (9%)
E. Mismatch repair defect (8%)

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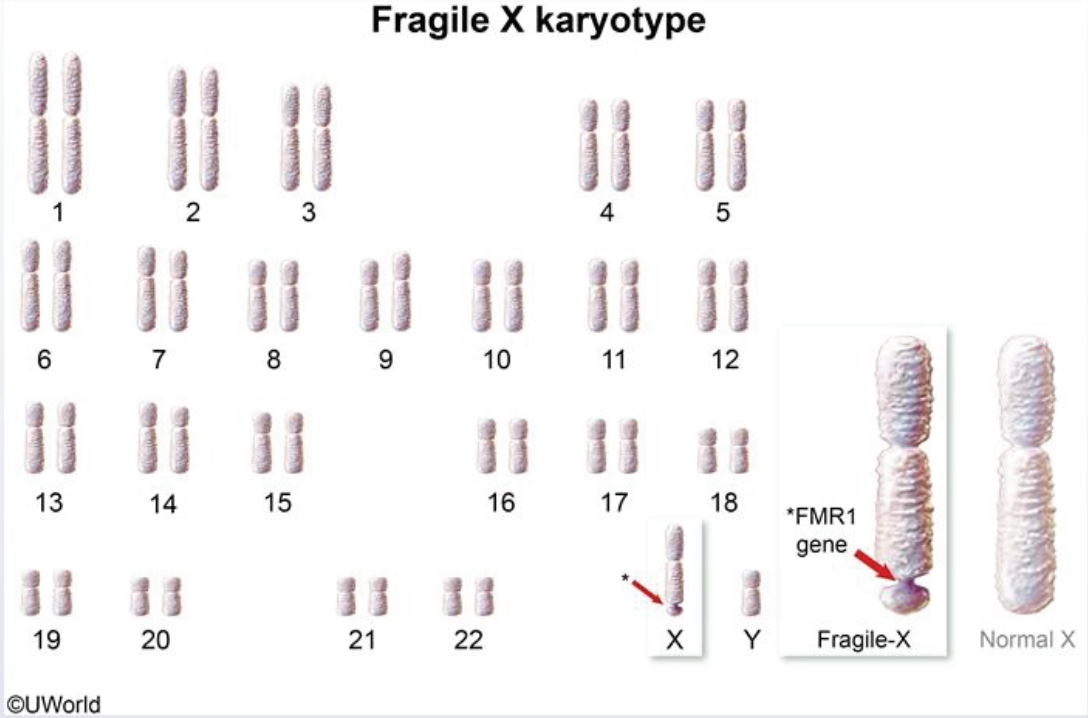


This patient has **fragile X syndrome** (FXS), the most common inherited cause of **intellectual disability**.



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This patient has **fragile X syndrome** (FXS), the most common inherited cause of **intellectual disability**. Physical findings include macroorchidism and dysmorphic facies (eg, long and narrow face, prominent forehead and chin). **Neuropsychiatric disorders** include developmental delay, attention deficit-hyperactivity disorder, and autism spectrum disorder (ASD). This patient's delayed language acquisition and poor social skills are suggestive of ASD.

FXS is caused by a mutation of the fragile X mental retardation 1 (*FMR1*) gene on the **long arm of the X chromosome**. *FMR1* normally has 5 to 55 CGG trinucleotide repeats and can potentially expand during **meiosis in oocytes**. "Full mutation" is characterized by **>200 CGG trinucleotide repeats**, which causes ***FMR1* hypermethylation**. DNA methylation **inactivates** *FMR1*, preventing transcription and production of fragile X mental retardation protein, thereby impairing neural development. Southern blot analysis is used to measure the degree of methylation and determine the number of CGG repeats.

**(Choices A and C)** Exons ("**ex**pressed cod**ons**") are protein coding regions of DNA. Introns are removed during intranuclear mRNA processing and not expressed in the final mRNA sequence. Abnormalities involving mRNA splicing do not play a role in FXS pathogenesis.

**(Choice D)** Imprinting refers to gene expression from only one parental allele, rather than from both. A



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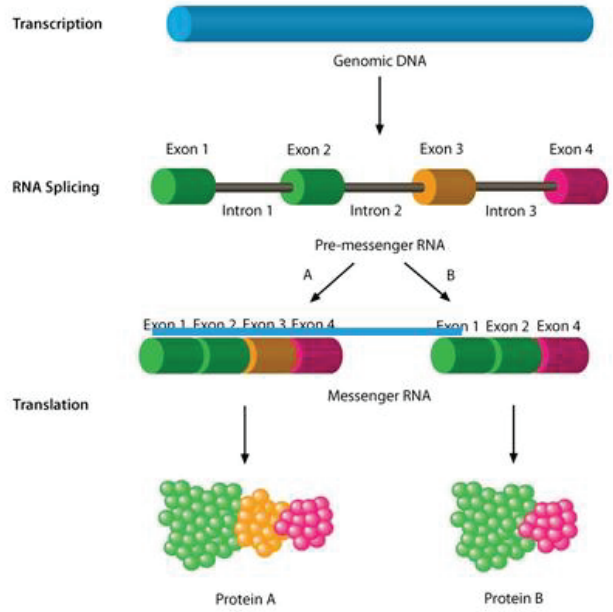


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**(Choice D)** Imprinting refers to gene expression from only one parental allele, rather than from both. A mutation in the preferentially expressed allele can result in Prader-Willi syndrome (PWS) or Angelman syndrome. PWS is caused by a paternally-inherited deletion of part of chromosome 15 while the maternal allele is not expressed. In contrast, Angelman syndrome is caused by a maternally-inherited deletion of the same portion of chromosome 15 while the paternal allele is not expressed.

**(Choice E)** Defects in DNA mismatch repair genes cause Lynch syndrome, a condition characterized by an increased risk of hereditary non-polyposis colorectal cancer and extraintestinal malignancies (eg, endometrial cancer).

**Educational objective:**

Fragile X syndrome is caused by an increased number of CGG trinucleotide repeats on the fragile X mental retardation 1 (*FMR1*) gene on the long arm of the X chromosome. This leads to hypermethylation and inactivation of *FMR1*.

**References**

- Fragile X syndrome
- FMR1: a gene with three faces
- Fragile X spectrum disorders



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(Choice D) Imprinting refers to gene expression from only one parental allele, rather than from both. A

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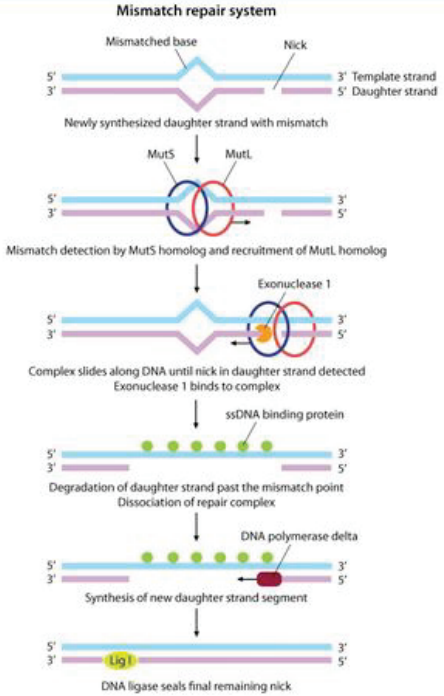


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Fragile X spectrum disorders



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A 12-year-old boy is brought to the emergency department by his mother due to right hand clumsiness. Several hours ago he attempted to climb a tree with a friend but lost his balance and fell from a branch. The boy tried to break the fall by grabbing the tree branch with his right hand. He landed safely on his feet with no head injury or loss of consciousness. On physical examination, he has difficulty performing fine finger movements with the right hand. Which of the following structures is most likely injured in this patient?

A. Axillary nerve
B. Long thoracic nerve
C. Lower trunk of the brachial plexus
D. Musculocutaneous nerve
E. Radial nerve
F. Suprascapular nerve

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A. Axillary nerve (4%)
B. Long thoracic nerve (1%)
C. Lower trunk of the brachial plexus (75%)
D. Musculocutaneous nerve (4%)
E. Radial nerve (14%)
F. Suprascapular nerve (0%)



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Brachial plexus

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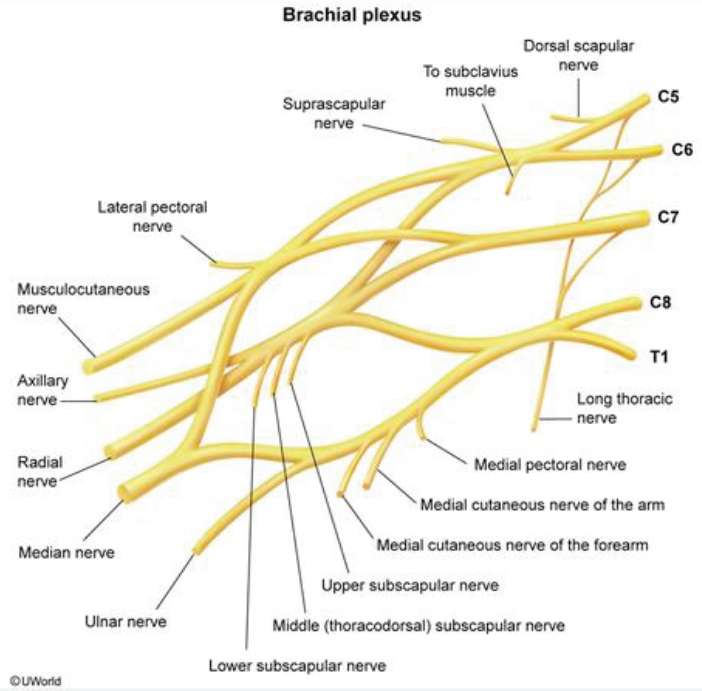


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Median nerve Medial cutaneous nerve of the forearm



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Lower subscapular nerve

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**Sudden upward jerking** of the arm at the shoulder can cause injury to the **lower trunk** of the brachial plexus. The lower trunk carries nerve fibers from the C8 and T1 spinal levels that ultimately contribute to the median and ulnar nerves. Together, these nerves innervate all of the intrinsic muscles of the hand (eg, lumbricals, interossei, thenar, hypothenar).

Injury to the lower trunk of the brachial plexus may cause paralysis of all the **intrinsic hand muscles (Klumpke's palsy)**. Weakness of lumbricals causes impaired flexion of the metacarpophalangeal joints and impaired extension of the interphalangeal joints. Relative sparing of the extrinsic flexors and extensors of the hand contributes to the **total claw hand deformity** seen in this condition. Sensory loss can also occur over the medial aspect of the hand/forearm. Involvement of the T1 nerve root proximal to the sympathetic trunk may cause concomitant Horner's syndrome (eg, ipsilateral ptosis, miosis, anhidrosis).

**(Choice A)** Shoulder dislocations or fractures of the proximal humerus can cause axillary nerve injury, which results in weakness of the deltoid and teres minor muscles.

**(Choice B)** Long thoracic nerve injury classically occurs during axillary lymph node dissection and results in paralysis of the serratus anterior muscle, leading to winging of the scapula.

**(Choice D)** Injury to the musculocutaneous nerve causes weakened elbow flexion because the nerve



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**(Choice B)** Long thoracic nerve injury classically occurs during axillary lymph node dissection and results in paralysis of the serratus anterior muscle, leading to winging of the scapula.

**(Choice D)** Injury to the musculocutaneous nerve causes weakened elbow flexion because the nerve innervates the biceps brachii and brachialis muscles.

**(Choice E)** Fractures at the midshaft of the humerus commonly cause radial nerve injury. Patients may experience posterior forearm and dorsolateral hand numbness with paralysis of the wrist and finger extensors (wrist drop).

**(Choice F)** The suprascapular nerve innervates the supraspinatus and infraspinatus muscles. Nerve injury may result in problems with abduction and lateral rotation of the arm, respectively.

**Educational objective:**

The lower trunk of the brachial plexus carries nerve fibers from the C8 and T1 spinal levels that are responsible for innervating all of the intrinsic muscles of the hand (via the median and ulnar nerves). Sudden upward stretching on the arm at the shoulder can damage the lower trunk, resulting in finger clumsiness with total claw hand deformity.

**References**

- Brachial plexopathy: a review of traumatic and nontraumatic causes.


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A 5-month-old boy is brought to the office by his parents who are concerned that he has developmental delay. He has 3 older siblings, and the parents report that his siblings were much more active and interactive at the boy's age. The family has just moved to the United States from South America and did not have consistent primary care previously. Physical examination shows that the boy is unable to roll from front to back or back to front and does not seem to recognize his parents. Comprehensive laboratory evaluation reveals impaired tetrahydrobiopterin synthesis. Which of the following is most likely deficient in this patient?

A. Acetylcholine
B. Gamma-aminobutyric acid
C. Glutamate
D. Phenylalanine
E. Serotonin

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C. Glutamate
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A. Acetylcholine (6%)
B. Gamma-aminobutyric acid (10%)
C. Glutamate (14%)
D. Phenylalanine (30%)
✓ E. Serotonin (37%)

37%
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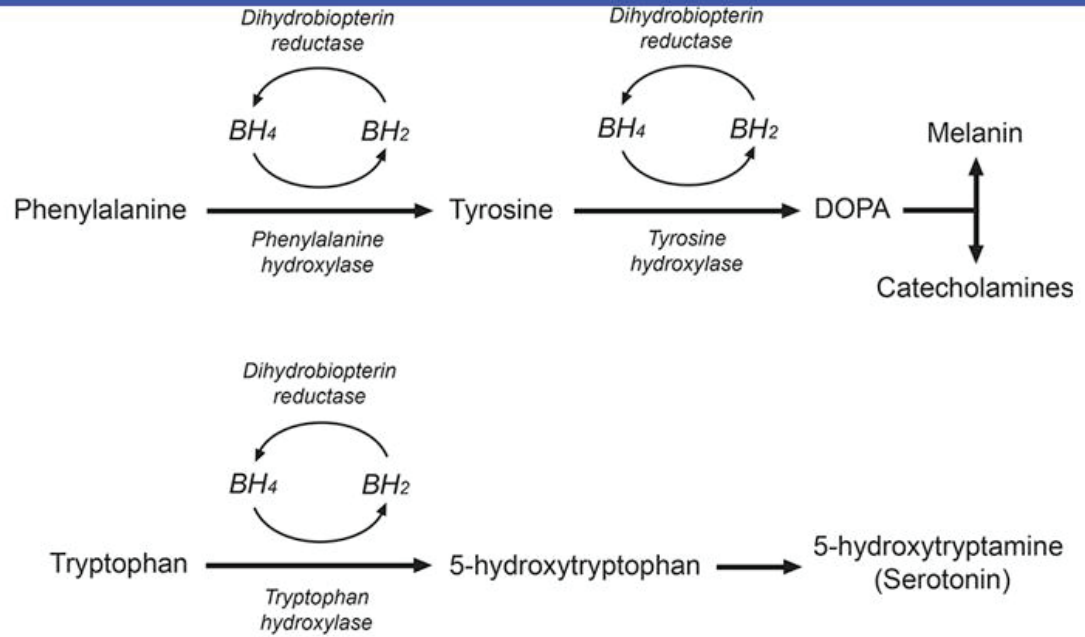


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Tetrahydrobiopterin ($BH_4$) is a cofactor in the synthesis of serotonin (a major neurotransmitter), tyrosine (a precursor of DOPA), and DOPA (the antecedent of the neurotransmitters dopamine, norepinephrine and epinephrine). Dihydropteridine reductase enzymatically reduces dihydrobiopterin ($BH_2$) to tetrahydrobiopterin ($BH_4$). Serotonin (5-hydroxytryptamine, or 5HT) is formed through hydroxylation and decarboxylation of the amino acid tryptophan.

Most cases of **phenylketonuria** are due to phenylalanine hydroxylase deficiency. Less commonly, the etiology is due to **$BH_4$ deficiency** secondary to **dihydropteridine reductase deficiency**. The consequences of defective phenylalanine and tryptophan metabolism are phenylalanine accumulation **(Choice D)** and **low levels of serotonin and other neurotransmitters**, respectively.

The combination of high phenylalanine levels, which may disrupt neuronal and glial development, and low serotonin and other neurotransmitters results in progressive **neurologic deterioration** in untreated patients. Manifestations include developmental delay, hypotonia, dystonia, and seizures. Treatment includes both a **low phenylalanine diet** and **$BH_4$ supplementation**.

**(Choice A)** Acetylcholine is a neuromuscular junction neurotransmitter synthesized from choline and acetyl-CoA by choline acetyltransferase. In myasthenia gravis, production of antibodies against



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includes both a **low phenylalanine diet** and **$BH_4$ supplementation**.

**(Choice A)** Acetylcholine is a neuromuscular junction neurotransmitter synthesized from choline and acetyl-CoA by choline acetyltransferase. In myasthenia gravis, production of antibodies against acetylcholine receptors leads to muscle weakness.

**(Choice B)** Gamma-aminobutyric acid (GABA) is an inhibitor of presynaptic transmission in the central nervous system that is formed by glutamate decarboxylation, a reaction catalyzed by glutamate decarboxylase. Phenobarbital, an antiepileptic medication, potentiates GABA activity to decrease or cease seizure activity.

**(Choice C)** Glutamate is an excitatory neurotransmitter that is synthesized from glutamine by the enzyme glutaminase. Ketamine is an N-methyl-D-aspartate (NMDA) receptor noncompetitive antagonist that blocks glutamate, which can result in anesthesia, sedation, and memory loss.

**Educational objective:**
Tetrahydrobiopterin ($BH_4$) is a cofactor used by hydroxylase enzymes in the synthesis of tyrosine, dopamine, and serotonin. Phenylketonuria can result from $BH_4$ deficiency due to dihydropteridine reductase deficiency. Intellectual disability is the hallmark of this condition and results in neurotransmitter (eg, serotonin) deficiency and hyperphenylalanemia. Treatment involves a low phenylalanine diet and $BH_4$



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acetyl-CoA by choline acetyltransferase. In myasthenia gravis, production of antibodies against acetylcholine receptors leads to muscle weakness.

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**Educational objective:**

Tetrahydrobiopterin ($BH_4$) is a cofactor used by hydroxylase enzymes in the synthesis of tyrosine, dopamine, and serotonin. Phenylketonuria can result from $BH_4$ deficiency due to dihydropteridine reductase deficiency. Intellectual disability is the hallmark of this condition and results in neurotransmitter (eg, serotonin) deficiency and hyperphenylalanemia. Treatment involves a low phenylalanine diet and $BH_4$ supplementation.

**References**



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order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 62-year-old woman has double vision, especially when reading at bedtime. The problem first started several months ago and was intermittent but has worsened over the last 2 weeks and now bothers her constantly. The patient has also developed difficulty chewing and swallowing foods. She usually feels better in the mornings. She has no extremity weakness or sensory symptoms. The patient has no other medical problems and takes no medications. She does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. BMI is 27 kg/m$^2$. Examination shows bilateral ptosis; there is weakness of adduction of the right eye and abduction of the left eye. Muscle strength is 4/5 in proximal muscles in the upper and lower extremities. Deep tendon reflexes are 2+ throughout.

**Item 1 of 2**

Which of the following changes involving the postsynaptic muscle cell most likely explains this patient's symptoms?

A. Impaired excitation-contraction coupling

B. Prolonged absolute refractory period

C. Reduced action potential amplitude



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constantly. The patient has also developed difficulty chewing and swallowing foods. She usually feels better in the mornings. She has no extremity weakness or sensory symptoms. The patient has no other medical problems and takes no medications. She does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. BMI is 27 kg/m$^2$. Examination shows bilateral ptosis; there is weakness of adduction of the right eye and abduction of the left eye. Muscle strength is 4/5 in proximal muscles in the upper and lower extremities. Deep tendon reflexes are 2+ throughout.

**Item 1 of 2**

Which of the following changes involving the postsynaptic muscle cell most likely explains this patient's symptoms?

A. Impaired excitation-contraction coupling
B. Prolonged absolute refractory period
C. Reduced action potential amplitude
D. Reduced action potential propagation velocity
E. Reduced amplitude of motor end plate potential


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are normal. BMI is 27 kg/m$^2$. Examination shows bilateral ptosis; there is weakness of adduction of the right eye and abduction of the left eye. Muscle strength is 4/5 in proximal muscles in the upper and lower extremities. Deep tendon reflexes are 2+ throughout.

**Item 1 of 2**

Which of the following changes involving the postsynaptic muscle cell most likely explains this patient's symptoms?

- A. Impaired excitation-contraction coupling (16%)
- B. Prolonged absolute refractory period (7%)
- ✗ C. Reduced action potential amplitude (11%)
- D. Reduced action potential propagation velocity (12%)
- ✓ E. Reduced amplitude of motor end plate potential (51%)

Incorrect
Correct answer

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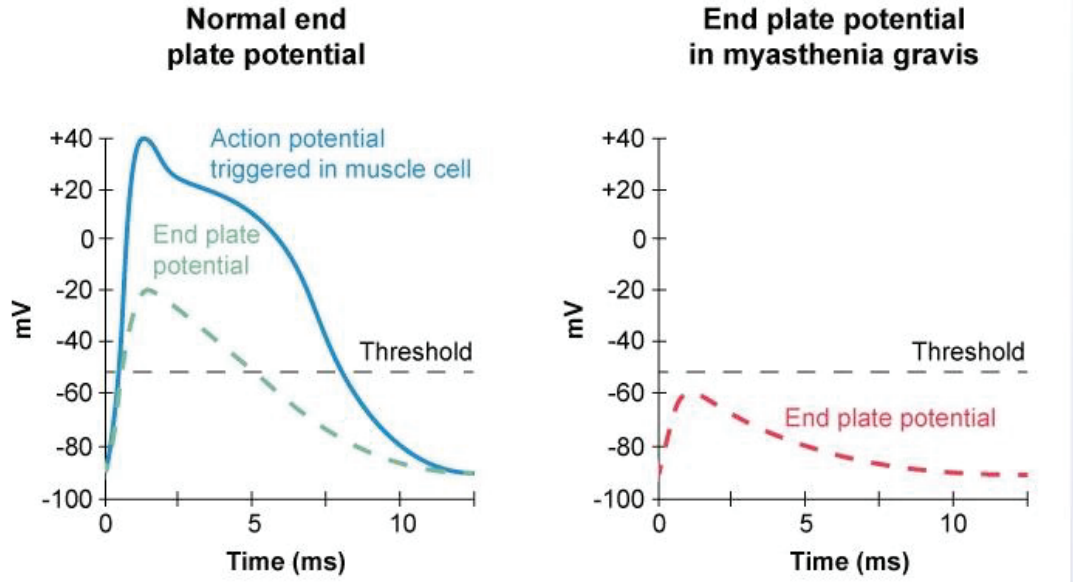


This patient with progressive diplopia and weakness with mastication (both worse at night), along with ptosis and proximal muscle weakness on examination, likely has **myasthenia gravis** (MG). This disease



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This patient with progressive diplopia and weakness with mastication (both worse at night), along with ptosis and proximal muscle weakness on examination, likely has **myasthenia gravis** (MG). This disease is characterized by:

- Fluctuating weakness of certain voluntary muscles, particularly those innervated by motor nuclei of the brainstem (eg, ocular and bulbar muscles)
- Progressive weakening over the course of the day or after exercise (fatigability)
- Decreased compound muscle action potential amplitude (the summed action potentials of all the muscle fibers in a motor unit) on electromyography with repeated excitation
- Rapid restoration of strength of affected muscles with rest
- Improvement in strength following the administration of cholinesterase inhibitors

MG is most commonly caused by autoantibodies against postsynaptic nicotinic acetylcholine receptors. Binding of antibody to these receptors results in blockade of the receptor's active site, receptor internalization and degradation, and damage to the motor end plate due to complement fixation. Overall, this leads to **decreased numbers of functional acetylcholine receptors** at the neuromuscular junction. The decrease in the number of available cation channels reduces the end plate potential following acetylcholine release. Because the **threshold potential is not reached**, the **muscle cells do not**


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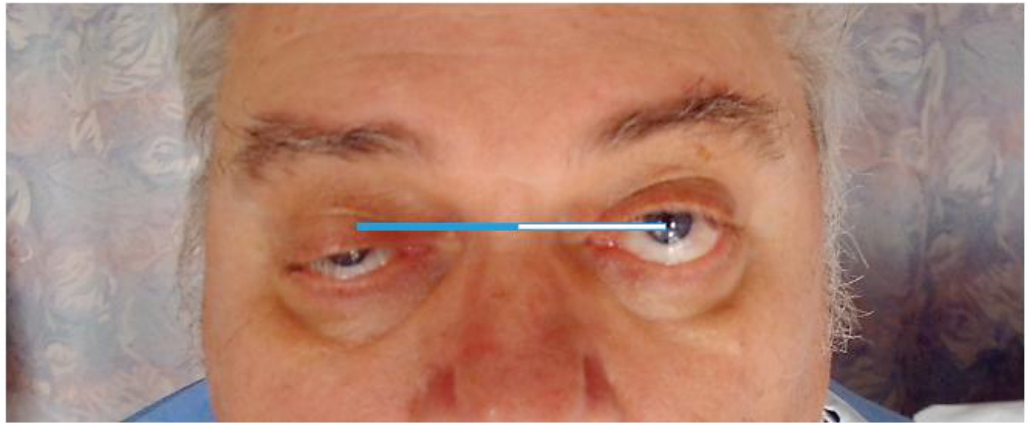

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acetylcholine release. Because the **threshold potential is not reached**, the **muscle cells do not**



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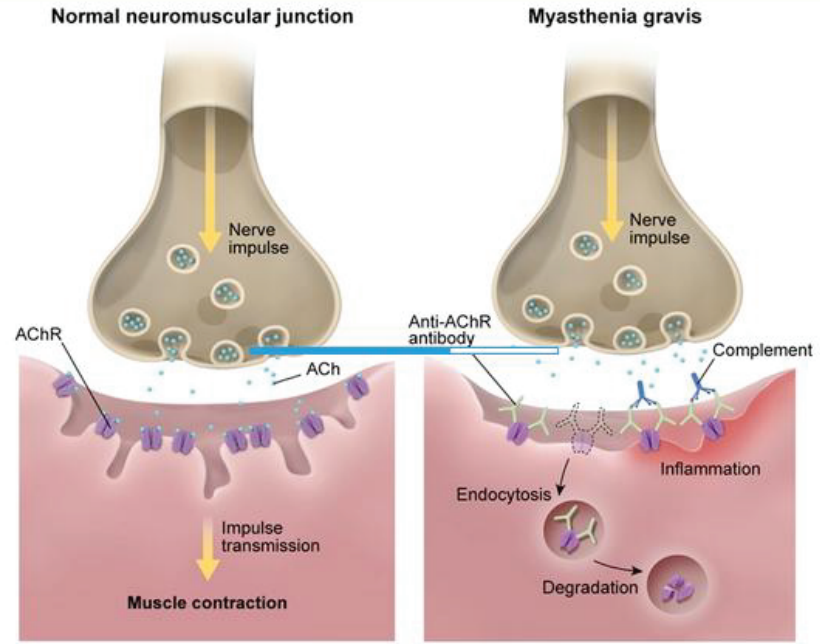


ACh = acetylcholine; AChR = acetylcholine receptor.

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acetylcholine release. Because the **threshold potential is not reached**, the **muscle cells do not**



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this leads to **decreased numbers of functional acetylcholine receptors** at the neuromuscular junction. The decrease in the number of available cation channels reduces the end plate potential following acetylcholine release. Because the **threshold potential is not reached**, the **muscle cells do not depolarize**. Synaptic concentrations of acetylcholine are unaffected, unlike in botulism or Lambert-Eaton syndrome.

**(Choice A)** Excitation-contraction coupling refers to the process whereby an action potential within the muscle cell causes contraction of the muscle. In skeletal muscle, this process proceeds by the release of calcium into the cytoplasm, which subsequently binds troponin C and induces a conformational change allowing actin and myosin to bind. Impaired coupling implies that an action potential occurs but the skeletal muscle is unable to contract (eg, impaired actin and myosin binding), whereas MG is caused by a failure to achieve the threshold for an action potential to occur.

**(Choice B)** The absolute refractory period for muscles in patients with MG is normal.

**(Choice C)** The action potential amplitude of the postsynaptic muscle cell is determined by the properties of the cell membrane and is not affected by the quality of the stimulus at the muscle end plate. This is not the same as compound muscle action potential, which decreases with repeated excitation in patients with MG due to depolarization of fewer myofibers.


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achieve the threshold for an action potential to occur.

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**(Choice D)** Once the threshold voltage is exceeded at the neuromuscular end plate, an action potential propagates at a velocity determined by the particular properties of the muscle cell membrane. In MG, the muscle cell membrane is not affected outside of the neuromuscular junction.

**Educational objective:**
Myasthenia gravis is an autoimmune disease that causes a decrease in the number of functional acetylcholine receptors within the neuromuscular junction. This reduces the number of postsynaptic cation channels that can open in response to acetylcholine, which reduces the amplitude of motor end plate potential and prevents muscle fiber depolarization.

Pathophysiology Nervous System Myasthenia gravis



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## Item 2 of 2

The patient is started on appropriate treatment and reports significant symptom improvement. However, she now has abdominal cramping, nausea, sweating, and diarrhea. Which of the following agents can be used to effectively control these new symptoms?

- A. Fluoxetine
- B. Glycopyrrolate
- C. Pilocarpine
- D. Prazosin
- E. Propranolol

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## Item 2 of 2

The patient is started on appropriate treatment and reports significant symptom improvement. However, she now has abdominal cramping, nausea, sweating, and diarrhea. Which of the following agents can be used to effectively control these new symptoms?

- A. Fluoxetine (4%)
- ✓ B. Glycopyrrolate (50%)
- C. ~~Pilocarpine~~ (31%)
- D. ~~Prazosin~~ (7%)
- E. ~~Propranolol~~ (5%)

Correct

50%
Answered correctly

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| Cholinergic toxicity | |
|---|---|
| Muscarinic effects **(DUMBELS)** | • **D**iarrhea/diaphoresis<br>• **U**rination<br>• **M**iosis<br>• **B**ronchospasm, bronchorrhea & bradycardia<br>• **E**mesis<br>• **L**acrimation<br>• **S**alivation |
| Nicotinic effects | • Muscle weakness, paralysis & fasciculations |

The treatment of **myasthenia gravis** typically involves the use of a cholinesterase inhibitor, an immunosuppressive agent, and possible thymectomy. This patient is most likely receiving treatment with a **cholinesterase inhibitor**, such as pyridostigmine, which inhibits the degradation of acetylcholine in the neuromuscular junction. This improves skeletal muscle weakness but can cause **muscarinic overstimulation** of the smooth muscles and excessive glandular secretions (eg, diarrhea, diaphoresis, abdominal cramping, emesis).


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abdominal cramping, emesis).

**Selective muscarinic antagonists** (eg, glycopyrrolate, hyoscyamine, propantheline) can be used to reduce the side effects of cholinesterase inhibitors in sites where acetylcholine action is mediated by muscarinic receptors (ie, gastrointestinal tract). Because of their selectivity, these drugs improve side effects without affecting the action of cholinesterase inhibitors on skeletal muscle, which uses nicotinic receptors.

**(Choice A)** Fluoxetine is a selective serotonin reuptake inhibitor used primarily in the treatment of depression. It acts in a fashion similar to the cholinesterase inhibitors in that it prolongs the activity of a neurotransmitter on its target tissue. However, it is otherwise unrelated to cholinesterase inhibitors or their effects.

**(Choice C)** Pilocarpine is a nonselective muscarinic receptor agonist. Use of this agent would worsen this patient's side effects.

**(Choices D and E)** Prazosin is an alpha-1 adrenergic antagonist, and propranolol is a beta adrenergic antagonist. Use of either agent does not prevent the side effects of a cholinesterase inhibitor.

**Educational objective:**
The treatment of myasthenia gravis involves the use of a cholinesterase inhibitor, immunosuppressants,



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**(Choice A)** Fluoxetine is a selective serotonin reuptake inhibitor used primarily in the treatment of depression. It acts in a fashion similar to the cholinesterase inhibitors in that it prolongs the activity of a neurotransmitter on its target tissue. However, it is otherwise unrelated to cholinesterase inhibitors or their effects.

**(Choice C)** Pilocarpine is a nonselective muscarinic receptor agonist. Use of this agent would worsen this patient's side effects.

**(Choices D and E)** Prazosin is an alpha-1 adrenergic antagonist, and propranolol is a beta adrenergic antagonist. Use of either agent does not prevent the side effects of a cholinesterase inhibitor.

**Educational objective:**
The treatment of myasthenia gravis involves the use of a cholinesterase inhibitor, immunosuppressants, and possible thymectomy. Cholinesterase inhibitors may cause adverse effects related to muscarinic overstimulation, which can be ameliorated by the use of an antimuscarinic agent such as glycopyrrolate, hyoscyamine, or propantheline.

| Pathophysiology | Nervous System | Myasthenia gravis |
|---|---|---|
| Subject | System | Topic |



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A study was conducted to determine the utility of adjunctive therapy in bacterial meningitis. Patients with acute bacterial meningitis whose cerebrospinal fluid (CSF) analysis showed gram-positive diplococci were divided into 2 groups. The first (control) group was given systemic antibiotics only, and the second (experimental) group was given dexamethasone followed by systemic antibiotics. Compared to the control group, patients in the experimental group developed fewer neurologic sequelae and had a lower risk of death. The experimental patients most likely benefited from the use of this drug due to which of the following?

A. Decreased cerebral metabolic activity
B. Decreased inflammatory response in the CSF
C. Increased antibiotic penetration into the CSF
D. Increased bone marrow release of neutrophils
E. Increased plasma glucose for cerebral use

Submit



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A study was conducted to determine the utility of adjunctive therapy in bacterial meningitis. Patients with acute bacterial meningitis whose cerebrospinal fluid (CSF) analysis showed gram-positive diplococci were divided into 2 groups. The first (control) group was given systemic antibiotics only, and the second (experimental) group was given dexamethasone followed by systemic antibiotics. Compared to the control group, patients in the experimental group developed fewer neurologic sequelae and had a lower risk of death. The experimental patients most likely benefited from the use of this drug due to which of the following?

A. ~~Decreased cerebral metabolic activity~~ (1%)
✓ B. Decreased inflammatory response in the CSF (83%)
C. ~~Increased antibiotic penetration into the CSF~~ (6%)
D. ~~Increased bone marrow release of neutrophils~~ (3%)
E. ~~Increased plasma glucose for cerebral use~~ (5%)

83% 52 secs 09/26/2020


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**Acute bacterial meningitis** is characterized by a massive **inflammatory response** in the central nervous system. The inflammation is driven by **bacterial subcapsular components**, particularly macromolecules of the bacterial cell wall such as teichoic acid and peptidoglycan. These components trigger the release of **inflammatory cytokines** (eg, tumor necrosis factor–alpha, interferon-gamma, interleukin 12), leading to loosening of the tight junctions of the blood-brain barrier, vasogenic edema, elevation of intracranial pressure, and recruitment of leukocytes.

***Streptococcus pneumoniae***, a gram-positive diplococcus, is the leading cause of acute bacterial meningitis in adults. Initial antibiotic therapy against *S pneumoniae* lyses the bacteria and releases cell wall components that increase cerebrospinal fluid (CSF) inflammatory cytokines. Studies have shown that pretreatment with **dexamethasone reduces the levels of inflammatory cytokines** in the CSF and limits risk of inflammation-induced morbidity (eg, seizures, focal neurologic deficits) and death. Other forms of bacterial meningitis, such as those due to *Neisseria meningitidis* and *Haemophilus influenzae*, do not benefit from glucocorticoid pretreatment, possibly because these gram-negative organisms have thinner cell walls (less peptidoglycan and no teichoic acid), resulting in less inflammatory cytokine release.

**(Choice A)** Therapeutic hypothermia (32-34 C [89.6-93.2 F]) can be used after hypoxic/ischemic brain injury due to cardiac arrest. It reduces cerebral metabolic activity and limits metabolic strain within



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cell walls (less peptidoglycan and no teichoic acid), resulting in less inflammatory cytokine release.

**(Choice A)** Therapeutic hypothermia (32-34 C [89.6-93.2 F]) can be used after hypoxic/ischemic brain injury due to cardiac arrest. It reduces cerebral metabolic activity and limits metabolic strain within damaged neurologic tissue. This has been shown to improve neurologic recovery and long-term outcomes.

**(Choice C)** The inflammatory response to bacterial components in the CSF loosens the tight junctions of the blood-brain barrier, which aids antibiotic penetration into the central nervous system. Dexamethasone reduces the inflammatory response and would be expected to decrease permeability of the blood-brain barrier.

**(Choice D)** Glucocorticoids promote the release of granulocytes from the bone marrow and the movement of neutrophils off the endothelial wall into the systemic circulation. This often leads to an increase in the circulating white blood cell count with delayed migration into infected tissues.

**(Choice E)** Glucocorticoids can cause a dose-dependent increase in fasting serum glucose levels due to stimulation of hepatic gluconeogenesis and inhibition of glucose uptake in adipose tissue.

**Educational objective:**

Pneumococcal meningitis is associated with massive cerebrospinal fluid inflammatory cytokine release in



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the blood-brain barrier, which aids antibiotic penetration into the central nervous system. Dexamethasone reduces the inflammatory response and would be expected to decrease permeability of the blood-brain barrier.

**(Choice D)** Glucocorticoids promote the release of granulocytes from the bone marrow and the movement of neutrophils off the endothelial wall into the systemic circulation. This often leads to an increase in the circulating white blood cell count with delayed migration into infected tissues.

**(Choice E)** Glucocorticoids can cause a dose-dependent increase in fasting serum glucose levels due to stimulation of hepatic gluconeogenesis and inhibition of glucose uptake in adipose tissue.

**Educational objective:**
Pneumococcal meningitis is associated with massive cerebrospinal fluid inflammatory cytokine release in response to bacterial cell wall components. Treatment with dexamethasone prior to antibiotic therapy has been shown to reduce inflammation and decrease the risk of adverse outcomes (eg, seizures, focal neurologic deficits) and death. Other forms of bacterial meningitis do not seem to benefit from glucocorticoid treatment.

Pathophysiology Nervous System Meningitis


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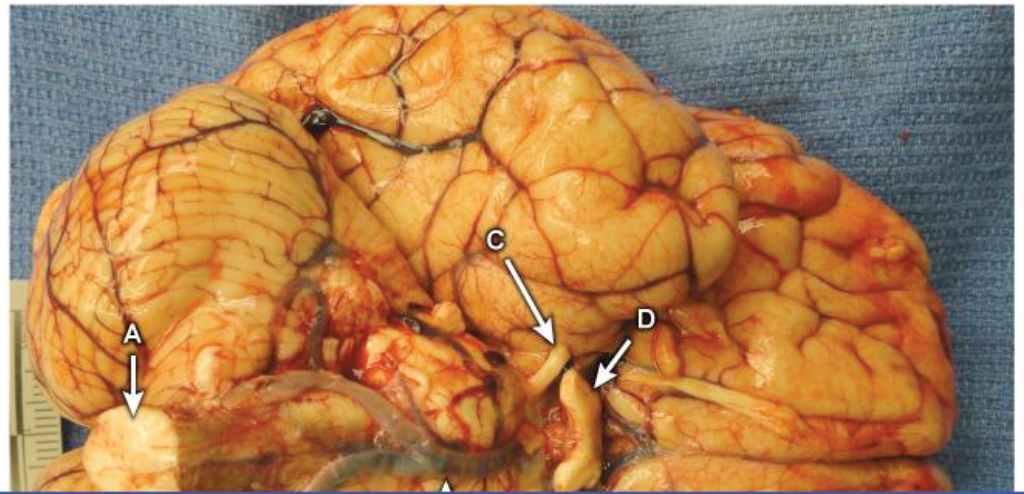
A 24-year-old man is brought to the emergency department due to seizures. He has had 2 days of worsening fever, headache, and vomiting. Physical examination shows signs of meningeal irritation. The patient rapidly becomes comatose and dies 48 hours later despite aggressive medical care. Autopsy examination shows congested leptomeninges with fibrinopurulent exudate (not shown). Microscopy reveals numerous ameba in the exudate and brain tissue. Which of the following is the most likely portal of entry of this pathogen into the CNS?



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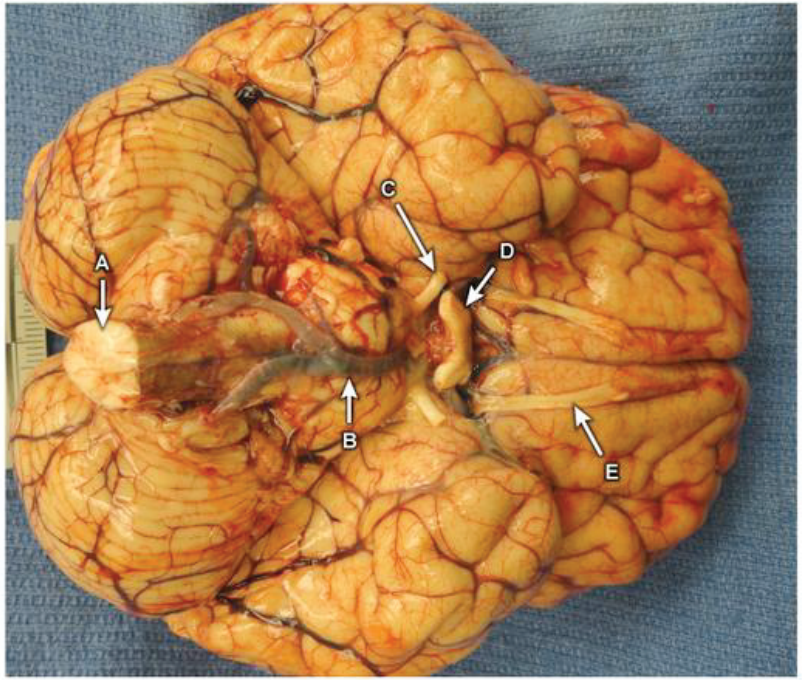


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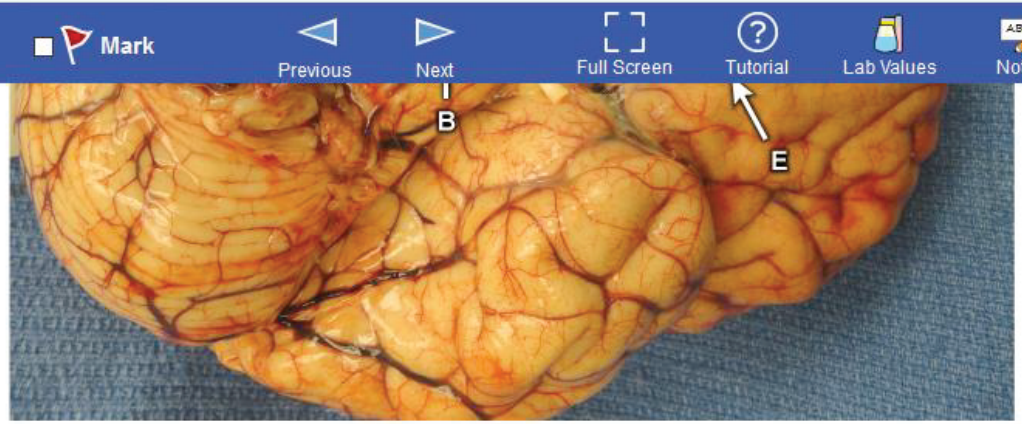


- A.A
- B.B
- C.C
- D.D
- E.E

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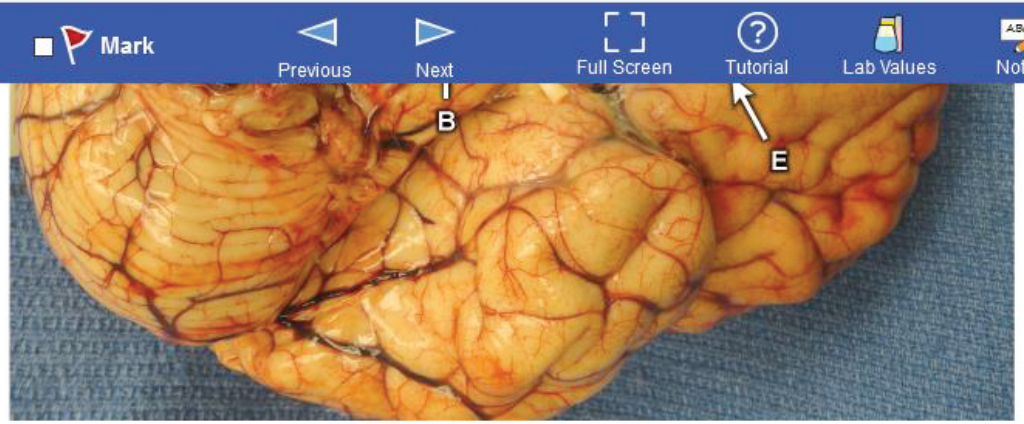


- A. A (5%)
- B. B (20%)
- C. C (3%)
- D. D (9%)
- ✓ E. E (60%)

Correct

60%

01 min, 01 sec

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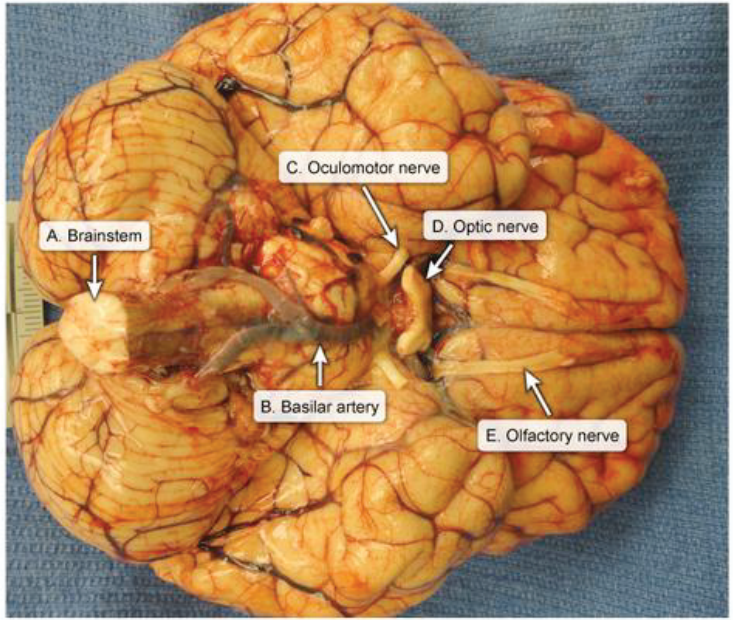
Labeled sections of the brain

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**Primary amebic meningoencephalitis** is a rare, highly fatal condition caused by the free-living, flagellated protozoan ***Naegleria fowleri***. This pathogen resides in **warm fresh water** (30-45 C) and moist soil. Humans are primarily exposed when the organism comes into contact with **nasal mucosa** during **recreational water activities** (eg, swimming, diving, water skiing, unchlorinated hot tub bathing). Although serologic evidence of exposure is widespread, only a small number of individuals develop invasive disease (~300 known cases).

Patients typically have rapidly progressive meningeal signs, cranial nerve deficits, and confusion. Cerebrospinal fluid analysis with wet mount can usually identify **motile trophozoites**. Although treatment should be attempted, almost all patients die within 2-3 days.

**(Choice A)** Rabies migrates centrally through peripheral nerves to the spinal cord and then rapidly ascends to the brain. Patients with rabies usually have preceding history of animal bite; furthermore, rabies is a virus, not an amoeba, and it generally presents with several days of constitutional symptoms followed by fever, hydrophobia, and pharyngeal spasm.

**(Choice B)** Most bacterial and fungal causes of meningitis enter the brain via the hematologic dissemination (eg, basilar artery). Although meningeal signs, vomiting, and headache frequently occur, amoebas would not be seen in the cerebrospinal fluid.


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is a virus, not an amoeba, and it generally presents with several days of constitutional symptoms followed by fever, hydrophobia, and pharyngeal spasm.

**(Choice B)** Most bacterial and fungal causes of meningitis enter the brain via the hematologic dissemination (eg, basilar artery). Although meningeal signs, vomiting, and headache frequently occur, amoebas would not be seen in the cerebrospinal fluid.

**(Choices C and D)** The oculomotor and optic nerve do not generally transmit infections into the brain; the herpes virus can travel via the trigeminal nerve (not labeled) into the brain, leading to temporal lobe encephalitis.

**Educational objective:**
Primary amebic encephalitis occurs when the free-living, motile protozoan *Naegleria fowleri* penetrates the olfactory mucosa and migrates in a retrograde fashion through the olfactory nerve to the brain. This rare, deadly infection primarily occurs after exposure to warm, fresh water during recreational activities.

| Microbiology | Nervous System | Meningitis |
|---|---|---|
| Subject | System | Topic |

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A 26-year-old man with a history of excessive daytime sleepiness due to narcolepsy enrolls in a clinical trial evaluating a new stimulant medication. The patient was previously treated with modafinil, but his symptoms did not improve. It is explained to the patient that the new drug works by promoting the release of dopamine and norepinephrine from nerve terminals in the central nervous system. Adverse effects of the drug are due primarily to excess release of norepinephrine from peripheral autonomic nerve terminals. Which of the following autonomic efferents would be most affected by the use of this drug?

A. Parasympathetic output to the bronchi
B. Parasympathetic output to the heart
C. Preganglionic sympathetic output
D. Sympathetic output to adrenal glands
E. Sympathetic output to eccrine sweat glands
F. Sympathetic output to the detrusor muscle

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A 26-year-old man with a history of excessive daytime sleepiness due to narcolepsy enrolls in a clinical trial evaluating a new stimulant medication. The patient was previously treated with modafinil, but his symptoms did not improve. It is explained to the patient that the new drug works by promoting the release of dopamine and norepinephrine from nerve terminals in the central nervous system. Adverse effects of the drug are due primarily to excess release of norepinephrine from peripheral autonomic nerve terminals. Which of the following autonomic efferents would be most affected by the use of this drug?

A. ~~Parasympathetic output to the bronchi~~ (1%)

B. ~~Parasympathetic output to the heart~~ (6%)

C. Preganglionic sympathetic output (12%)

D. Sympathetic output to adrenal glands (24%)

✗ E. Sympathetic output to eccrine sweat glands (16%)

✓ F. Sympathetic output to the detrusor muscle (39%)

Incorrect



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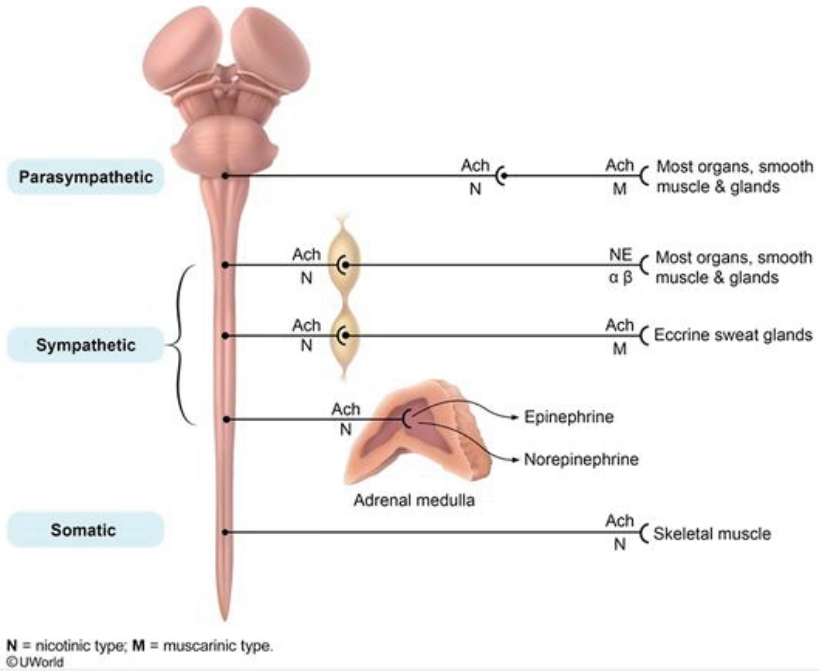
## Neurotransmitters




N = nicotinic type; M = muscarinic type.
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The parasympathetic and sympathetic subdivisions of the autonomic nervous system regulate most visceral functions of the body via 2-neuron signal transmission. In the parasympathetic system, preganglionic neurons arise from cranial nerve nuclei (eg, CN III, VII, IX, X) and from the sacral spinal cord and release acetylcholine, which binds to postganglionic nicotinic receptors found within the parasympathetic ganglia in or near the walls of target organs. Postganglionic neurons also release acetylcholine, activating muscarinic receptors within the target organs (eg, bronchi, heart) **(Choices A and B)**.

In the **sympathetic** system, preganglionic neurons arise from the thoracolumbar spinal cord and release acetylcholine, which binds to postganglionic nicotinic receptors in the sympathetic chain and prevertebral ganglia **(Choice C)**. **Postganglionic** neurons then release **norepinephrine**, activating alpha/beta receptors within target organs (including the bladder); however, there are 2 notable **exceptions** to this scheme:

1. The chromaffin cells of the **adrenal medulla** release norepinephrine and epinephrine directly into the circulation after stimulation by acetylcholine released from sympathetic preganglionic neurons **(Choice D)**.
2. The preganglionic and postganglionic sympathetic neurons that supply eccrine **sweat glands** are both cholinergic **(Choice E)**.



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**D)**.

2. The preganglionic and postganglionic sympathetic neurons that supply eccrine **sweat glands** are both cholinergic **(Choice E)**.

Among the answer choices, only sympathetic output to the detrusor muscle (provided by postganglionic neurons that release norepinephrine) would be significantly affected by the medication. Autonomic output to all the other mentioned structures is mediated by acetylcholine.

**Educational objective:**

The sympathetic nervous system typically regulates visceral function via 2-neuron signal transmission involving cholinergic preganglionic neurons and adrenergic postganglionic neurons. Eccrine sweat glands and the adrenal medullae are exceptions to this rule as they are both innervated by cholinergic neurons. The parasympathetic system uses both preganglionic and postganglionic cholinergic neurons.

**References**

- Physiology of the autonomic nervous system.

| Pharmacology | Nervous System | Autonomic nervous system |
|---|---|---|
| Subject | System | Topic |



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A 65-year-old male is undergoing rehabilitation after a stroke. Ten days ago, he presented to the emergency department with abrupt onset of left upper and lower extremity weakness. He has a history of hypertension, hypercholesterolemia, gastroesophageal reflux disease and hypothyroidism. He does not use tobacco, alcohol or illicit drugs. His blood pressure is 140/90 mm Hg and pulse is 72/min. He has weakness and increased tone in the left upper and lower extremities. You prescribe diazepam to this patient in order to decrease muscle spasticity of involved extremities. This patient should primarily be cautioned to avoid which of the following drugs?

- A. Chlorpheniramine
- B. Loratadine
- C. Acetaminophen
- D. Ranitidine
- E. Lansoprazole
- F. Folic acid



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emergency department with abrupt onset of left upper and lower extremity weakness. He has a history of hypertension, hypercholesterolemia, gastroesophageal reflux disease and hypothyroidism. He does not use tobacco, alcohol or illicit drugs. His blood pressure is 140/90 mm Hg and pulse is 72/min. He has weakness and increased tone in the left upper and lower extremities. You prescribe diazepam to this patient in order to decrease muscle spasticity of involved extremities. This patient should primarily be cautioned to avoid which of the following drugs?

- A. Chlorpheniramine (43%)
- B. Loratadine (9%)
- C. Acetaminophen (12%)
- D. Ranitidine (19%)
- E. Lansoprazole (14%)
- F. Folic acid (1%)

Correct

43%

56 secs

02/01/2021



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Diazepam is a long-acting benzodiazepine indicated as follows:

1. As an **anxiolytic**, it is effective for the management of generalized anxiety disorder and panic attacks.
2. The **sedative-hypnotic** effect of diazepam is useful for the short-term treatment of insomnia.
3. As an **anticonvulsant**, diazepam is indicated for status epilepticus. It is a first-line agent (along with chlordiazepoxide) for the treatment of seizures associated with alcohol withdrawal.
4. As a **muscle relaxant**, diazepam can stop the spasticity caused by upper motor neuron disorders (multiple sclerosis, strokes, spinal cord trauma) and tetanus.

The most common side effect of diazepam is sedation. Diazepam may also impair coordination and balance (sometimes avoided in the elderly for fear of falls), decrease memory and concentration, and produce confusion. These effects are amplified by the co-administration of other CNS-depressants. As a class, all benzodiazepines should be excluded from use in conjunction with alcohol, barbiturates, neuroleptics, or 1st generation antihistamines.

Among drugs listed in the answer choices, only chlorpheniramine causes sedation and should not be used with diazepam. Chlorpheniramine is a 1st generation antihistamine that acts by blocking both central and peripheral H1 receptors. Chlorpheniramine and other 1st generation antihistamines can be very sedating



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with diazepam. Chlorpheniramine is a 1st generation antihistamine that acts by blocking both central and peripheral H1 receptors. Chlorpheniramine and other 1st generation antihistamines can be very sedating because they easily penetrate the blood-brain barrier and accumulate in the CNS. The most sedating of this generation of antihistamines are diphenhydramine (Benadryl), promethazine, and hydroxyzine. Despite the associated sedation, these antihistamines are often still used to prevent/treat allergic reactions and motion sickness and as antiemetics.

**(Choice B)** Loratadine is a second-generation antihistamine that blocks peripheral H1 histamine receptors. It does not enter the CNS and does not cause drowsiness.

**(Choice D)** Ranitidine is a H2 receptor antagonist that inhibits gastric acid secretion. It has a slight affinity to the CYP450 enzyme, but studies have shown that ranitidine does not have clinically significant interactions with diazepam.

**(Choice E)** Lansoprazole is a proton pump inhibitor that decreases gastric acid secretion. Although both diazepam and lansoprazole are metabolized by the P450 system, studies have shown that lansoprazole does not have clinically significant interactions with diazepam.

**Educational objective:**

First generation H1-histamine receptor antagonists, including diphenhydramine and chlorpheniramine, can


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**(Choice B)** Loratadine is a second-generation antihistamine that blocks peripheral H1 histamine receptors. It does not enter the CNS and does not cause drowsiness.

**(Choice D)** Ranitidine is a H2 receptor antagonist that inhibits gastric acid secretion. It has a slight affinity to the CYP450 enzyme, but studies have shown that ranitidine does not have clinically significant interactions with diazepam.

**(Choice E)** Lansoprazole is a proton pump inhibitor that decreases gastric acid secretion. Although both diazepam and lansoprazole are metabolized by the P450 system, studies have shown that lansoprazole does not have clinically significant interactions with diazepam.

**Educational objective:**
First generation H1-histamine receptor antagonists, including diphenhydramine and chlorpheniramine, can cause significant sedation, especially when used with other medications that cause CNS depression (such as benzodiazepines).

**References**

- Influence of lansoprazole treatment on diazepam plasma concentrations
- Ranitidine does not impair oxidative or conjugative metabolism: noninteraction with antipyrine,


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MPTP is a toxic substance that induces a Parkinsonism-like syndrome by destroying dopaminergic neurons in the CNS. A series of experiments demonstrated that MPTP per se is minimally toxic. Actually, it is a metabolite of MPTP, produced by MAO type B and called MPP+, that causes the neurological damage. Pretreatment by which of the following agents would minimize the damage induced by MPTP consumption?

A. Amantadine
B. Levodopa
C. Levodopa/carbidopa
D. Selegiline
E. Pergolide

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MPTP is a toxic substance that induces a Parkinsonism-like syndrome by destroying dopaminergic neurons in the CNS. A series of experiments demonstrated that MPTP per se is minimally toxic. Actually, it is a metabolite of MPTP, produced by MAO type B and called MPP+, that causes the neurological damage. Pretreatment by which of the following agents would minimize the damage induced by MPTP consumption?

A. ~~Amantadine~~ (5%)
B. ~~Levodopa~~ (2%)
C. Levodopa/carbidopa (9%)
✓ D. Selegiline (79%)
E. Pergolide (3%)

Correct

79%
Answered correctly

01 min, 06 secs
Time Spent

01/09/2021
Last Updated



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Selegiline is an inhibitor of MAO, type B. Since the actual causative agent of MPTP-associated Parkinsonism-type symptoms is formed by MAO, type B, pretreatment with selegiline can prevent this damage to dopaminergic neurons. Clinically, selegiline is used to delay the progression of Parkinson disease.

**(Choice A)** Amantadine was designed as an antiviral influenza agent, but it is also known to have dopaminergic activity and possibly anticholinergic action as well; therefore, it may provide moderate improvement in patients with Parkinson disease. Amantadine and anticholinergic agents may produce undesirable side effects such as dry mouth, nausea, vomiting, blurring of vision, visual hallucinations, and other mental changes; they should be used with caution in the elderly.

**(Choice B)** Dopamine is absent in the nigrostriatum of patients with Parkinson disease. Dopamine itself cannot be directly administered because it is unable to cross the blood-brain barrier. Levodopa, or L-dopa, is the immediate precursor of dopamine. It is taken up by the brain, engulfed in the striatum by cell processes that have cell bodies in the substantia nigra; then, in the substantia nigra, L-dopa is converted to dopamine, and released as a neurotransmitter.

**(Choice C)** Levodopa is a dopamine analog that remains the most effective treatment for symptoms of



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**(Choice C)** Levodopa is a dopamine analog that remains the most effective treatment for symptoms of Parkinson disease. Levodopa is absorbed in the small intestine via a large, neutral-amino-acid transporter system and is then converted to dopamine by the enzyme dopa-decarboxylase. Peripheral conversion to dopamine is largely responsible for the nausea and vomiting associated with L-dopa use. The addition of dopa-decarboxylase inhibitors (carbidopa) that do not cross the blood-brain barrier decrease the peripheral formation of dopamine, relieving the intense nausea and vomiting caused by levodopa alone.

**(Choice E)** Pergolide is a dopamine agonist which directly stimulates dopamine D2 receptors. It provides only modest improvement in parkinsonian symptoms when used as monotherapy; however, this modest improvement may be sufficient to delay the introduction of levodopa by months or years, thus delaying levodopa-related side effects.

**Educational Objective:**

1. Selegiline is an inhibitor of MAO, type B and can prevent MPTP-induced damage of dopaminergic neurons.
2. Selegiline is used clinically to delay the progression of Parkinson disease.
3. Many neurologists favor the use of combinations of selegiline, anticholinergics, and amantadine until they no longer provide control of symptoms. Only then is levodopa/carbidopa introduced.



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A 32-year-old woman, gravida 1 para 0, at 35 weeks gestation comes to the emergency department due to absent fetal movement for the past 24 hours. The patient has had no prenatal care. Fetal ultrasonography confirms an intrauterine fetal demise. Autopsy examination of the fetus reveals incomplete separation of the cerebral hemispheres with a single ventricle, as shown in the image below:

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Which of the following is most closely associated with this fetal condition?

A. Congenital rubella syndrome

B. Intrauterine Zika virus infection

C. Maternal lithium use

D. Trisomy 13

E. Trisomy 21

Submit



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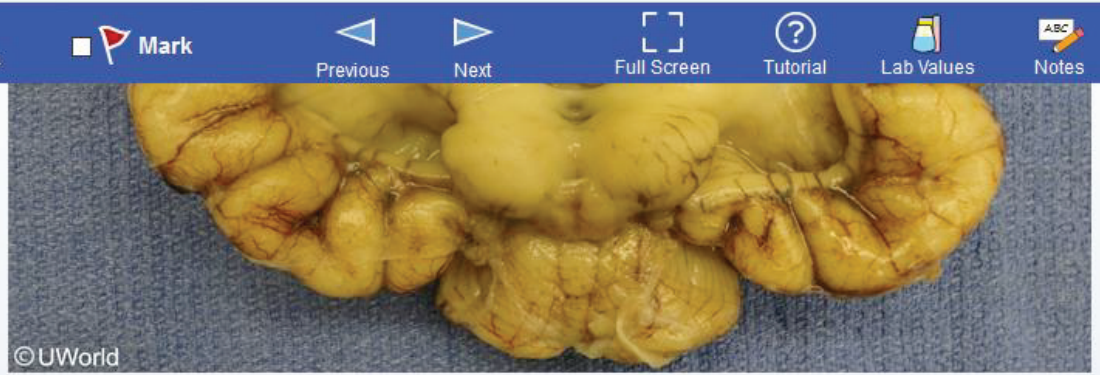


Which of the following is most closely associated with this fetal condition?

A. Congenital rubella syndrome (4%)

B. Intrauterine Zika virus infection (19%)

C. Maternal lithium use (6%)

D. Trisomy 13 (67%)

E. Trisomy 21 (1%)

Correct

67%

13 secs

02/03/2021



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| Holoprosencephaly | |
|---|---|
| **Embryology** | • Incomplete forebrain (prosencephalon) division into 2 hemispheres |
| **Etiologies** | • Genetic: Trisomy 13, sonic hedgehog gene mutations<br>• Environmental: maternal alcohol use, retinoic acid |
| **Clinical features** | • CNS abnormalities<br>◦ Range from asymptomatic to seizures, severe intellectual disability, death<br>• Midface abnormalities<br>◦ Range from mild hypotelorism and cleft lip/palate to cyclopia, primitive nose, facial cleft |

Fetal brain development begins at week 3, when the ectodermal cells thicken and invaginate to form the neural tube, which differentiates into the primitive forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon). The prosencephalon gives rise to the diencephalon, which develops into the thalamus and third ventricle, and telencephalon, which develops into the **cerebral hemispheres** and **lateral ventricles**.

This fetus has an **incomplete separation** of the cerebral hemispheres with a single lateral ventricle



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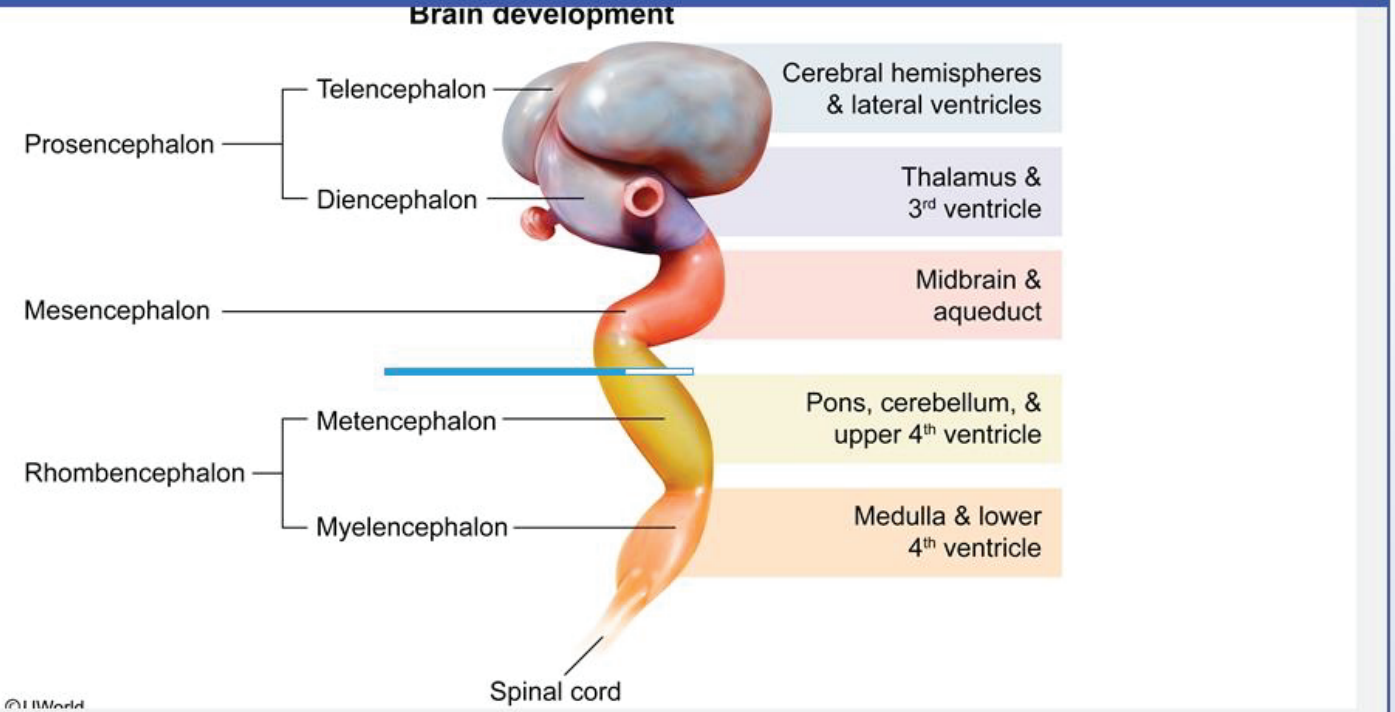


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This fetus has an incomplete separation of the cerebral hemispheres with a single lateral ventricle.



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This fetus has an **incomplete separation** of the cerebral hemispheres with a single lateral ventricle consistent with **holoprosencephaly**, a condition in which the forebrain fails to completely divide into right and left hemispheres. Disease severity and midline facial malformations (eg, facial clefts, cyclopia) are dependent upon the degree of hemisphere division; mild forms can be asymptomatic whereas severe cases can be lethal (as in this case).

Holoprosencephaly may be due to a variety of factors (eg, sonic hedgehog gene mutations); the most common associated chromosomal abnormality is **trisomy 13** (Patau syndrome). Other midline defects of trisomy 13 include microcephaly, microphthalmia, cleft lip/palate, and omphalocele. Cardiac abnormalities are also common, and cutis aplasia (scalp defect) is characteristic. The majority of affected fetuses die in utero.

**(Choice A)** Congenital rubella syndrome may be fatal in utero or present in neonates with the characteristic triad of sensorineural hearing loss, cataracts, and congenital heart disease (eg, patent ductus arteriosus). Although CNS infection can result in microcephaly, holoprosencephaly is rare.

**(Choice B)** Zika virus infection in utero causes infection of neural progenitor cells, resulting in impaired fetal brain development. Due to the destruction of the neurons, patients with congenital Zika virus infection typically have microcephaly, intracranial calcifications (a sign of tissue necrosis), and ventriculomegaly;



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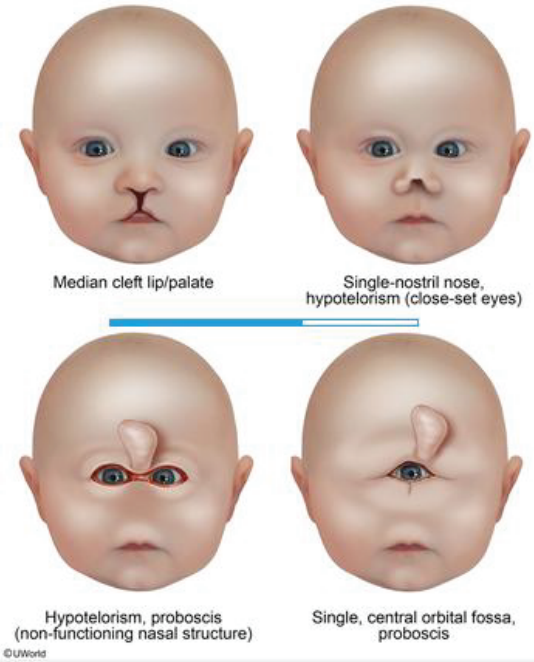
Holoprosencephaly spectrum

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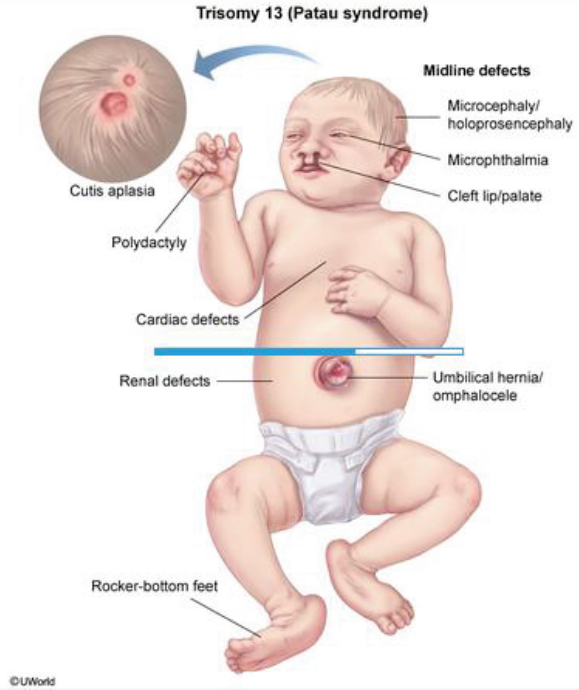


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characteristic triad of sensorineural hearing loss, cataracts, and congenital heart disease (eg, patent ductus arteriosus). Although CNS infection can result in microcephaly, holoprosencephaly is rare.

**(Choice B)** Zika virus infection in utero causes infection of neural progenitor cells, resulting in impaired fetal brain development. Due to the destruction of the neurons, patients with congenital Zika virus infection typically have microcephaly, intracranial calcifications (a sign of tissue necrosis), and ventriculomegaly; holoprosencephaly is uncommon with Zika infection.

**(Choice C)** Maternal lithium use is classically associated with fetal cardiac abnormalities (eg, Ebstein anomaly), not neurologic structural defects.

**(Choice E)** Trisomy 21 (Down syndrome) can cause ventriculomegaly and decreased brain volume, but patients still have 2 separate cerebral hemispheres and ventricles (not holoprosencephaly).

**Educational objective:**
Holoprosencephaly is due to failure of the primitive forebrain (prosencephalon) to divide into the right and left hemispheres, resulting in a spectrum of brain and midface abnormalities (eg, facial clefts, cyclopia). Trisomy 13 is the most commonly associated etiology.

**References**

- Syndromes associated with holoprosencephaly.



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characteristic triad of sensorineural hearing loss, cataracts, and congenital heart disease (eg, patent ductus

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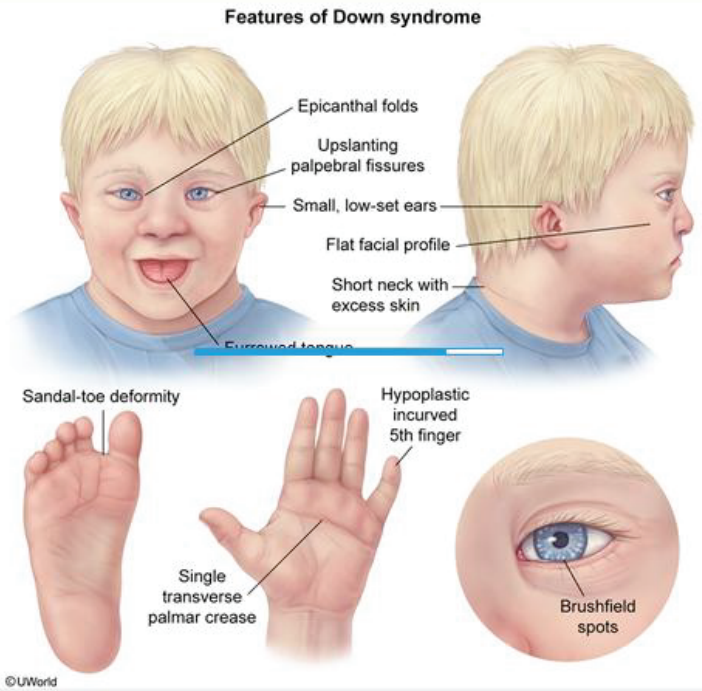


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A 64-year-old woman is brought to the emergency department due to stroke-like symptoms. The patient has a history of transient ischemic attacks as well as other risk factors for cerebrovascular disease, including hypertension, type 2 diabetes mellitus, and hyperlipidemia. Urgent brain imaging reveals occlusion of a vessel indicated by the arrow in the exhibit. Which of the following findings is most likely to be observed in this patient?

A. Down-and-out right eye with impaired extraocular movements
B. Left-sided motor weakness, including lower facial region
C. Loss of conjugate lateral gaze on both sides
D. Sensory loss over the right side of the face and left side of the body
E. Vision loss over the left half of the visual field in both eyes

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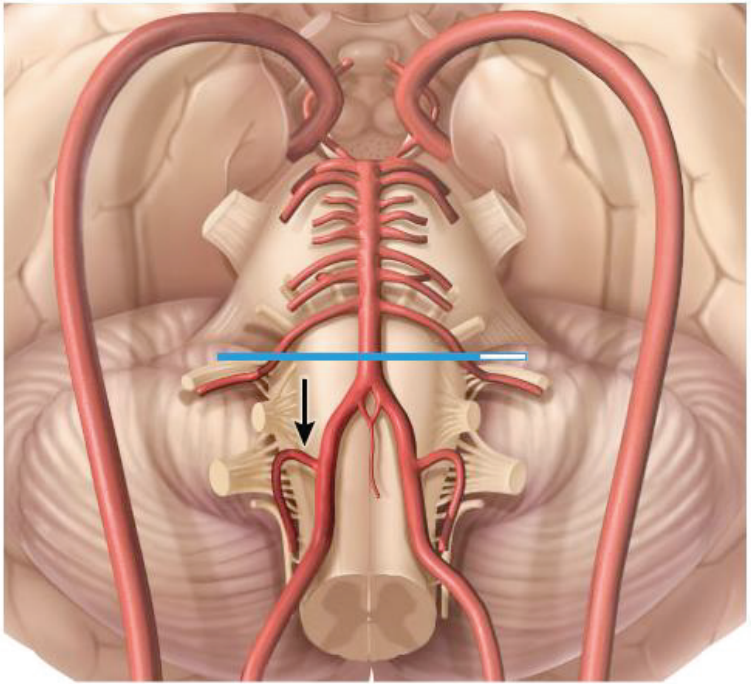

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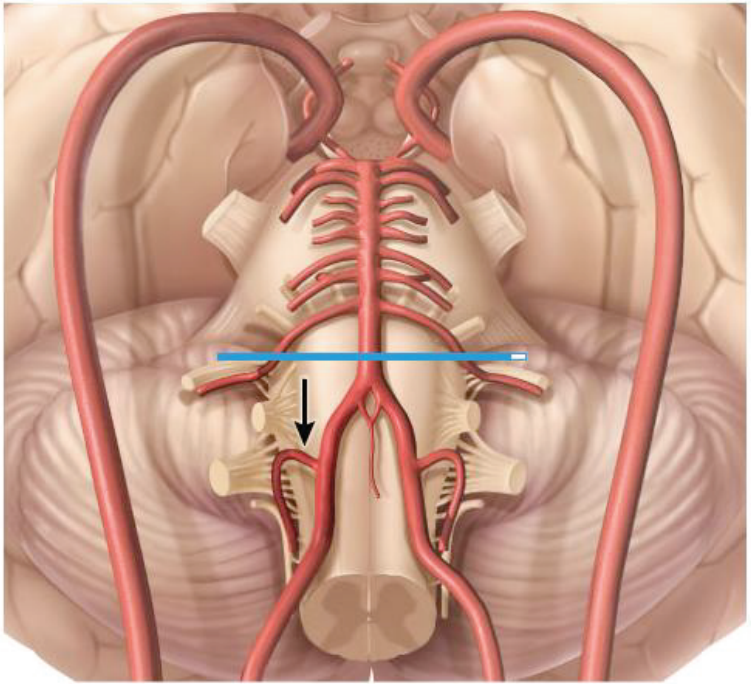

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A 64-year-old woman is brought to the emergency department due to stroke-like symptoms. The patient has a history of transient ischemic attacks as well as other risk factors for cerebrovascular disease, including hypertension, type 2 diabetes mellitus, and hyperlipidemia. Urgent brain imaging reveals occlusion of a vessel indicated by the arrow in the exhibit. Which of the following findings is most likely to be observed in this patient?

A. Down-and-out right eye with impaired extraocular movements (6%)

B. Left-sided motor weakness, including lower facial region (23%)

C. Loss of conjugate lateral gaze on both sides (7%)

✓ D. Sensory loss over the right side of the face and left side of the body (54%)

E. ~~Vision loss over the left half of the visual field in both eyes~~ (8%)

Correct

54%
Answered correctly

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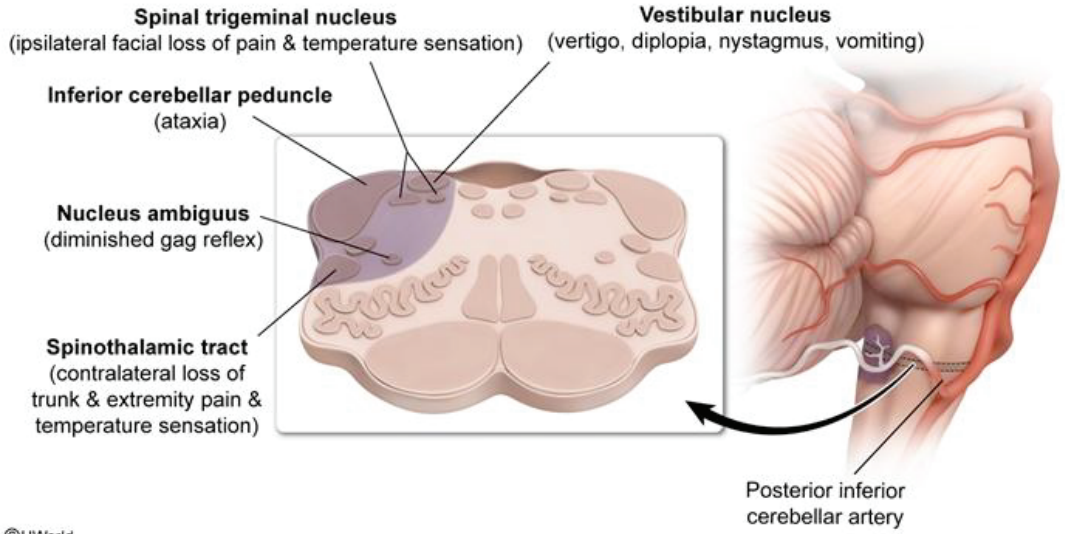
## Lateral medullary (Wallenberg) syndrome

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vertebral artery. Occlusion of the PICA results in **lateral medullary (Wallenberg) syndrome**. This



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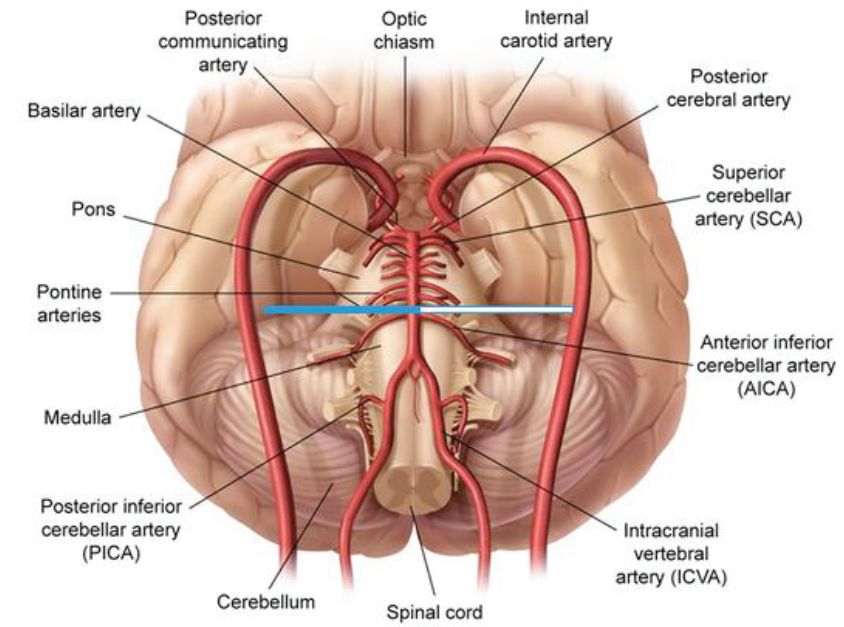
Exhibit Display

Posterior brain circulation

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vertebral artery. Occlusion of the PICA results in **lateral medullary (Wallenberg) syndrome**. This



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This patient has occlusion of the right posterior inferior cerebellar artery (PICA), which arises from the vertebral artery. Occlusion of the PICA results in **lateral medullary (Wallenberg) syndrome**. This disorder classically results in a constellation of symptoms because of damage to specific areas:

- Vertigo and nystagmus (vestibular nucleus)
- Ataxia (inferior cerebellar peduncle)
- Loss of pain and temperature sensation in the ipsilateral face (spinal trigeminal nucleus) and contralateral body (spinothalamic tract)
- Bulbar weakness (eg, dysphagia, dysarthria) (nucleus ambiguus)

Horner syndrome (ie, miosis, ptosis, anhidrosis) may also occur in the ipsilateral eye due to damage to descending sympathetic nervous system fibers.

**(Choice A)** Damage to the oculomotor nerve (CN III) can lead to impaired extraocular movements with a down-and-out eye due to unopposed action of the superior oblique muscle (innervated by the trochlear nerve [CN IV]) and the lateral rectus muscle (innervated by the abducens nerve [CN VI]). When this finding (ie, down-and-out eye) is accompanied by contralateral lower facial weakness and hemiplegia, the underlying cause can be midbrain infarction due to occlusion of the posterior cerebral artery (ie, Weber



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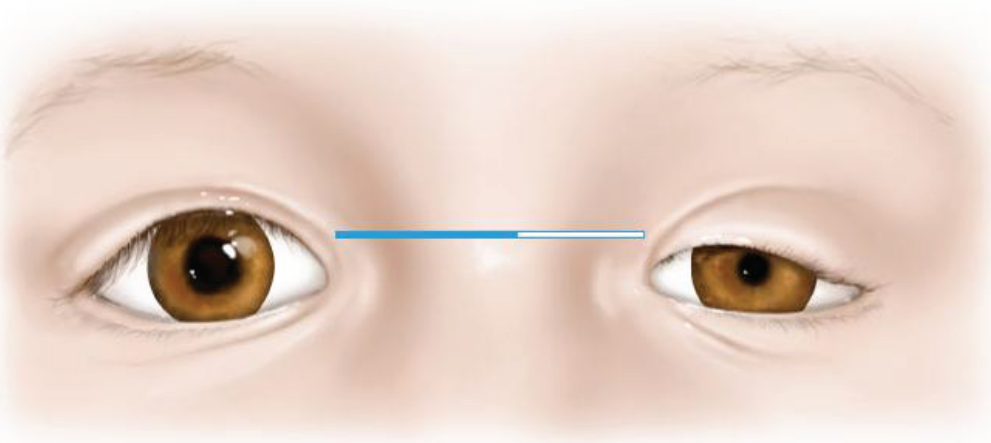
cerebellar artery

Exhibit Display

## Horner syndrome



Normal eye

Ptosis, miosis

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syndrome).

**(Choice B)** Weakness of the face, arm, and leg is classically caused by contralateral motor cortex or internal capsule infarction due to occlusion of the middle cerebral artery.

**(Choice C)** Internuclear ophthalmoplegia (ie, loss of conjugate lateral gaze) is caused by damage to the medial longitudinal fasciculus, which can occur with occlusion of the pontine artery. Bilateral loss of conjugate gaze is more likely with other etiologies (eg, multiple sclerosis plaques) because bilateral ischemic injury to the same area is uncommon.

**(Choice E)** Homonymous hemianopia (ie, vision loss in the same half of the visual field in both eyes) with macular sparing is classically caused by occlusion of the posterior cerebral artery; the macula is spared due to collateral blood supply from the middle cerebral artery. Homonymous hemianopia without macular sparing can occur due to damage of the optic tract or optic radiation, which can occur with occlusion of several different vessels (eg, anterior choroidal, middle cerebral artery).

**Educational objective:**
Posterior inferior cerebellar artery occlusion causes lateral medullary (Wallenberg) syndrome. This disorder is characterized by vertigo/nystagmus, ipsilateral cerebellar signs, loss of pain/temperature sensation in the ipsilateral face and contralateral body, bulbar weakness, and ipsilateral Horner syndrome


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**(Choice C)** Internuclear ophthalmoplegia (ie, loss of conjugate lateral gaze) is caused by damage to the medial longitudinal fasciculus, which can occur with occlusion of the pontine artery. Bilateral loss of conjugate gaze is more likely with other etiologies (eg, multiple sclerosis plaques) because bilateral ischemic injury to the same area is uncommon.

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**Educational objective:**

Posterior inferior cerebellar artery occlusion causes lateral medullary (Wallenberg) syndrome. This disorder is characterized by vertigo/nystagmus, ipsilateral cerebellar signs, loss of pain/temperature sensation in the ipsilateral face and contralateral body, bulbar weakness, and ipsilateral Horner syndrome.

| Anatomy | Nervous System | Ischemic stroke |
|---|---|---|
| Subject | System | Topic |

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A 36-year-old male is undergoing a major surgical procedure under general anesthesia. A fluorinated inhaled anesthetic (isoflurane) is used to achieve the desirable depth of central nervous system depression. An increase in which of the following parameters is most likely to happen during the anesthesia in this patient?

A. Glomerular filtration rate (GFR)
B. Effective renal plasma flow
C. Left ventricular ejection fraction (EF)
D. Hepatic blood flow
E. Cerebral blood flow

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A 36-year-old male is undergoing a major surgical procedure under general anesthesia. A fluorinated inhaled anesthetic (isoflurane) is used to achieve the desirable depth of central nervous system depression. An increase in which of the following parameters is most likely to happen during the anesthesia in this patient?

A. Glomerular filtration rate (GFR) (7%)
B. Effective renal plasma flow (7%)
C. Left ventricular ejection fraction (EF) (7%)
D. Hepatic blood flow (14%)
✓ E. Cerebral blood flow (62%)

Correct
62% Answered correctly
26 secs Time Spent
01/30/2021 Last Updated



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General anesthesia encompasses loss of consciousness, analgesia, amnesia, skeletal muscle relaxation and inhibition of reflexes. This complex of symptoms occurs due to the inhibition of electrical activity of neurons. Most of inhalation anesthetics, barbiturates, and benzodiazepines achieve CNS depression by influencing GABA receptors and increasing the inhibitory action of GABA. Inhaled anesthetics have also been shown to affect potassium channels in the neuronal membranes and lock them in the state of hyperpolarization. They may also affect nicotinic and glycine receptors.

Apart from their desirable action on CNS, inhalation anesthetics affect almost all organ systems of the body.

1. Cardiovascular effects include myocardial depression that leads to a decrease in cardiac output and an increase in atrial and ventricular pressures. Hypotension associated with fluorinated anesthetics is a result of decrease in cardiac output.
2. Respiratory: all inhalation anesthetics, except nitrous oxide, are respiratory depressants. They decrease tidal volume and minute ventilation and cause hypercapnia. Another undesirable effect is the suppression of mucociliary clearance, which may predispose to postoperative atelectasis. Halothane and sevoflurane have bronchodilation properties and are preferred in patients with asthma.
3. In the brain, fluorinated anesthetics decrease vascular resistance and lead to an increase in cerebral


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3. In the brain, fluorinated anesthetics decrease vascular resistance and lead to an increase in cerebral blood flow. It is an undesirable effect as it results in increased intracranial pressure.
4. In kidneys, inhaled anesthetics decrease glomerular filtration rate, increase renal vascular resistance and decrease renal plasma flow.
5. Fluorinated anesthetics decrease hepatic blood flow.

**(Choices A and B)** Renal function in general anesthesia is characterized by decrease in glomerular filtration rate and decrease in renal plasma flow.

**(Choice C)** Fluorinated anesthetics are myocardial depressants. They decrease cardiac output which leads to hypotension.

**(Choice D)** Fluorinated anesthetics decrease hepatic blood flow.

**Educational Objective:**
Almost all volatile anesthetics increase cerebral blood flow. It is an undesirable effect as it results in increased ICP. Other important effects of inhalation anesthetics are myocardial depression, hypotension, respiratory depression and decreased renal function.

Pharmacology | Nervous System | Anesthesia



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A 62-year-old, right-handed man is evaluated for an episode of left leg weakness that spontaneously resolved within 30 minutes of onset. The patient also has had transient vision loss in the right eye. Medical history is significant for hypertension and diabetes mellitus. Evaluation reveals an atherosclerotic plaque in the extracranial portion of the supplying artery. During percutaneous stenting of the lesion, the vascular catheter is inserted into the right common femoral artery and gradually advanced to the level of the aortic arch. Which of the following is the most likely path of the catheter before stenting of the culprit lesion can be performed?

A. Aorta → brachiocephalic artery → common carotid artery → external carotid artery

B. Aorta → brachiocephalic artery → common carotid artery → internal carotid artery

C. Aorta → common carotid artery → external carotid artery

D. Aorta → common carotid artery → internal carotid artery

E. Aorta → subclavian artery → vertebral artery

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A 62-year-old, right-handed man is evaluated for an episode of left leg weakness that spontaneously resolved within 30 minutes of onset. The patient also has had transient vision loss in the right eye. Medical history is significant for hypertension and diabetes mellitus. Evaluation reveals an atherosclerotic plaque in the extracranial portion of the supplying artery. During percutaneous stenting of the lesion, the vascular catheter is inserted into the right common femoral artery and gradually advanced to the level of the aortic arch. Which of the following is the most likely path of the catheter before stenting of the culprit lesion can be performed?

A. Aorta → brachiocephalic artery → common carotid artery → external carotid artery (12%)

✓ B. Aorta → brachiocephalic artery → common carotid artery → internal carotid artery (63%)

C. Aorta → common carotid artery → external carotid artery (5%)

D. Aorta → common carotid artery → internal carotid artery (17%)

E. Aorta → subclavian artery → vertebral artery (2%)

63% 30 secs 01/09/2021



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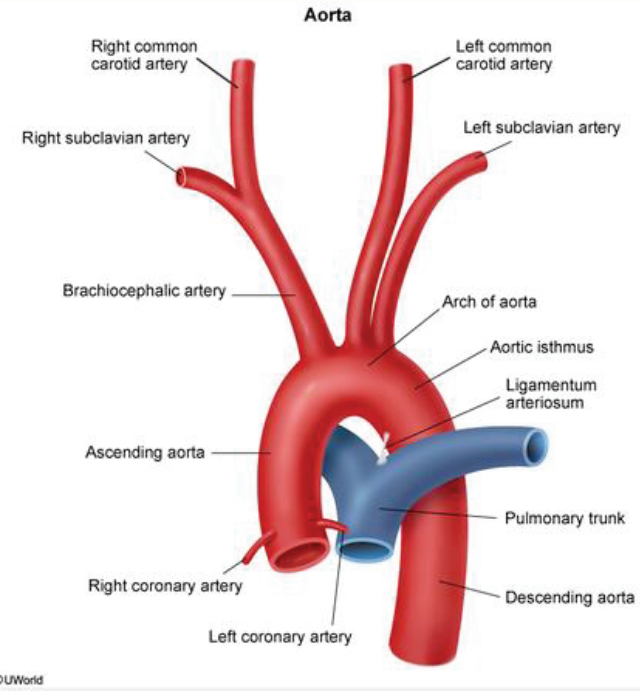


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This patient is having transient episodes of focal neurologic impairment, concerning for **transient ischemic attacks** (TIA), which often occur due to emboli originating from atherosclerotic plaques. The internal carotid artery supplies blood to the cerebral hemispheres, including the motor cortex, which controls the contralateral limbs. However, the ophthalmic artery, which gives rise to the retinal artery, originates from the ipsilateral internal carotid artery. Therefore, the combination of **left leg weakness** and **vision loss in the right eye** (amaurosis fugax) suggests a lesion in the **right internal carotid artery**.

Because TIAs are a risk factor for future stroke, intervention is warranted. After cannulation of the femoral artery, the catheter is advanced through the **aorta**. From there, the catheter can access much of the cerebrovascular circulation. The left common carotid and subclavian arteries branch directly from the aortic arch. However, on the right, the **brachiocephalic (innominate) artery** branches from the aortic arch then divides into the right subclavian and **right common carotid**. The common carotid then divides into the external carotid, which supplies blood to the face and neck, and the **internal carotid**, which supplies blood to the brain.

**(Choice A)** This is the path to the right external carotid artery. However, the external carotid artery supplies blood to the face and neck, not to the brain or retina.



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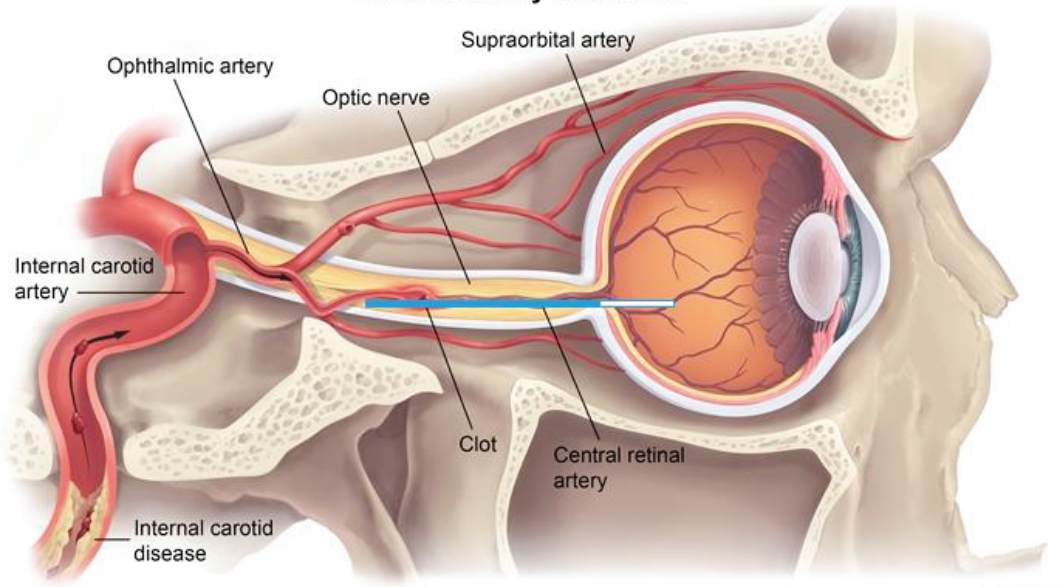
## Retinal artery occlusion

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supplies blood to the face and neck, not to the brain or retina.

**(Choices C and D)** The left common carotid artery branches directly from the aortic arch, then divides into the left internal and external carotid arteries. However, this patient's left leg weakness and vision loss in the right eye suggest a lesion in the right internal carotid artery.

**(Choice E)** This is the correct path to access the vertebral arteries, which supply the upper spinal cord, brainstem, cerebellum, and posterior part of the brain, rather than the motor cortex and the eye, which are affected in this patient.

**Educational objective:**

Transient ischemic attacks resulting in left leg weakness and vision loss in the right eye are likely due to emboli originating from the right internal carotid artery. The brachiocephalic artery branches from the aortic arch, then divides into the right subclavian and right common carotid arteries. The left common carotid and left subclavian arteries branch directly from the aortic arch.

| Anatomy | Nervous System | Carotid artery stenosis |
|---|---|---|
| Subject | System | Topic |

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supplies blood to the face and neck, not to the brain or retina.

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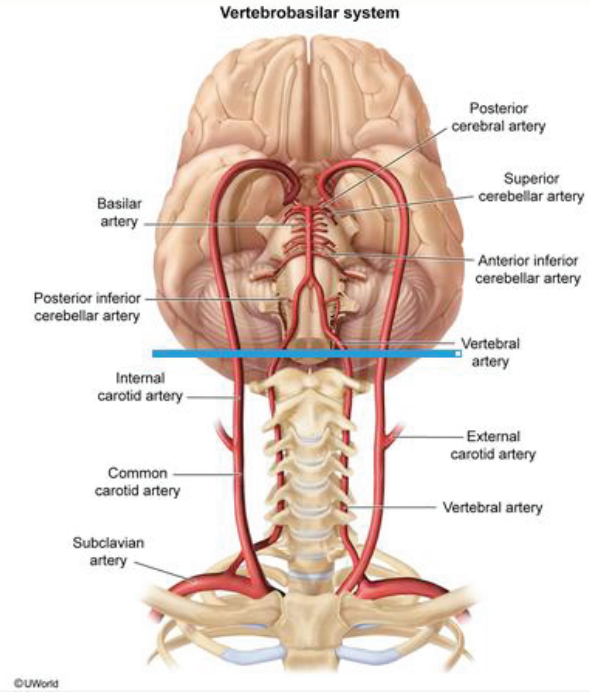


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A 34-year-old man is evaluated in the clinic due to difficulty walking over the past 2 weeks. His symptoms have resulted in several recent falls, but he has had no head trauma or loss of consciousness. He has never had these symptoms before. The patient is frustrated as he cannot carry out his duties as a mailman. He has a history of crack cocaine use in the distant past but no current illicit drug use. The patient is in a monogamous relationship but previously had numerous sexual partners. The physician asks him to stand with his feet close together, arms to the sides, and eyes closed. This maneuver most likely tests for abnormalities in which of the following?

A. Cortical sensory integration
B. Gait
C. Motor coordination
D. Muscle strength
E. Proprioception

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A. Cortical sensory integration (9%)
B. Gait (5%)
C. Motor coordination (6%)
D. Muscle strength (0%)
E. Proprioception (77%)

77%  59 secs  02/08/2021



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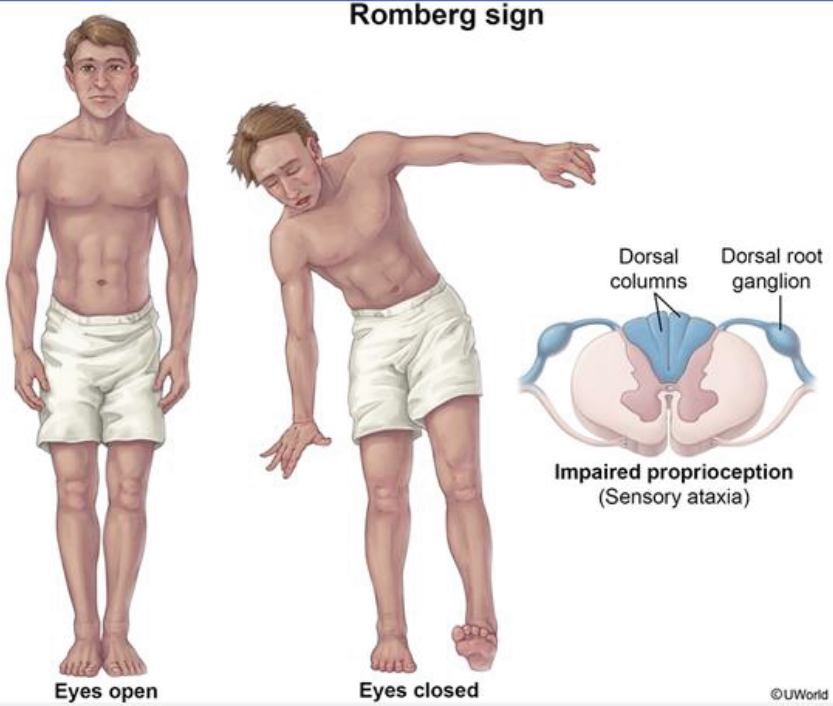
## Romberg sign

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The **Romberg test** is a test of **proprioception** used to distinguish sensory from cerebellar ataxia. The maneuver is executed by first instructing the patient to stand with the feet close together, arms to the sides, and eyes open. During this time, the patient is observed for unsteadiness. If the patient is unable to maintain this stance easily, some form of ataxia (cerebellar or sensory) is likely present.

To differentiate sensory from cerebellar ataxia, the patient is asked to close the eyes while maintaining the aforementioned posture. Removing the visual input forces the patient to rely on input from proprioceptive receptors in the trunk and extremities for posture maintenance. Failure to maintain this posture with the eyes closed is referred to as a positive Romberg sign and indicates **sensory ataxia**. Sensory ataxia may be caused by defects in the **posterior column** or **peripheral nerves**, which are classically caused by tabes dorsalis (syphilis) or vitamin $B_{12}$ deficiency.

Patients who show little or no change in their unsteadiness with their eyes closed (negative Romberg sign) likely have cerebellar ataxia due to impaired motor coordination. Cerebellar function/motor coordination is typically evaluated with rapid alternating movements, finger-to-nose testing, and heel-to-shin testing **(Choice C)**.

**(Choice A)** The parietal association cortex is an area that integrates multisensory (eg, visual, tactile,


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**(Choice A)** The parietal association cortex is an area that integrates multisensory (eg, visual, tactile, verbal) information to comprehend events and generate responses. Lesions in the nondominant hemisphere typically cause contralateral neglect, anosognosia (lack of awareness of illness), and constructional apraxia (inability to draw objects). Patients are tested by being asked to draw a clock or bisect a horizontal line.

**(Choice B)** Gait is tested by observing the patient walk casually, in tandem, on the heels, and on the toes. The patient should be assessed for speed, stride length, step height, and arm swing.

**(Choice D)** Muscle strength is tested directly by having the patient press or pull against resistance. Muscle strength is graded on a scale of 0-5 (0=no contraction, 3=contraction able to overcome gravity, 5=normal).

**Educational objective:**

The Romberg test is a test of proprioception in which patients are observed for unsteadiness as they stand with their feet close together, arms to the sides, and eyes closed. Failure to maintain this posture indicates sensory ataxia, which may be caused by defects in the posterior column or peripheral nerves (eg, tabes dorsalis, vitamin $B_{12}$ deficiency).

**References**



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A 26-year-old man comes to the office due to severe headaches that are increasing in frequency. The patient describes episodic, right-sided hemicranial throbbing or pulsating headaches accompanied by nausea and photophobia. The headaches began when he was in high school, but lately they have become more frequent and are affecting his work. The patient takes nonsteroidal analgesics and sumatriptan for the pain and metoclopramide for nausea. He has no other medical conditions and no drug allergies. Vital signs are within normal limits, and physical examination shows no abnormalities. A recent brain imaging study was normal. Which of the following pharmacotherapies would be most helpful to prevent recurrences of this patient's headache?

A. Capsaicin
B. Ergotamine
C. Hydrochlorothiazide
D. Sertraline
E. Topiramate



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patient describes episodic, right-sided hemicranial throbbing or pulsating headaches accompanied by nausea and photophobia. The headaches began when he was in high school, but lately they have become more frequent and are affecting his work. The patient takes nonsteroidal analgesics and sumatriptan for the pain and metoclopramide for nausea. He has no other medical conditions and no drug allergies. Vital signs are within normal limits, and physical examination shows no abnormalities. A recent brain imaging study was normal. Which of the following pharmacotherapies would be most helpful to prevent recurrences of this patient's headache?

A. Capsaicin (3%)
B. Ergotamine (25%)
C. Hydrochlorothiazide (0%)
D. Sertraline (8%)
✓ E. Topiramate (62%)

Correct
62%
01 min, 28 secs
09/21/2020


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| Migraine therapy | |
|---|---|
| **Abortive** | • Triptans<br>• NSAIDs, acetaminophen<br>• Antiemetics<br>• Ergotamine |
| **Preventive** | • Anticonvulsants (topiramate or valproate)<br>• Beta blockers<br>• Antidepressants (tricyclic or venlafaxine) |

**NSAIDs** = nonsteroidal anti-inflammatory drugs.

This patient has recurrent **migraine**, a disorder characterized by severe, unilateral headaches, frequently associated with nausea and sensitivity to light and sound. Migraine therapy is divided into abortive therapy for acute pain control and preventive therapy to reduce the frequency and severity of the headaches. Commonly used **abortive medications** include mild analgesics (eg, nonsteroidal anti-inflammatory drugs, acetaminophen), triptans (eg, sumatriptan), antiemetics (eg, metoclopramide, prochlorperazine), and ergotamines. These medications reduce symptoms at headache onset but do not prevent further


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ergotamines. These medications reduce symptoms at headache onset but do not prevent further headaches.

Patients with frequent migraines or significant impairment due to the symptoms warrant **preventive therapy**. **Topiramate** is an anticonvulsant that reduces the frequency of migraines. Other preventive medications include **beta blockers** (eg, metoprolol, propranolol), **tricyclic antidepressants** (eg, amitriptyline), and other anticonvulsants (eg, valproate).

**(Choice A)** Capsaicin is derived from chili peppers and is useful as a topical therapy for neuropathic or musculoskeletal pain; it is not useful for treatment of migraine.

**(Choice B)** Ergotamine has both agonist and antagonist activities on multiple neurotransmitters (eg, dopamine, serotonin, epinephrine) and acts as a vasoconstrictor. It is used for migraine abortion, not prevention.

**(Choice C)** Hydrochlorothiazide is an antihypertensive that reduces sodium reabsorption in the distal convoluted tubule. Although beta blockers (another type of antihypertensive) are useful for migraine prevention, hydrochlorothiazide is not indicated for treatment of migraines.

**(Choice D)** Sertraline is a selective serotonin reuptake inhibitor (SSRI) used for depression and anxiety. Although tricyclic antidepressants are used for migraine prevention, SSRIs have not been shown to prevent



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dopamine, serotonin, epinephrine) and acts as a vasoconstrictor. It is used for migraine abortion, not prevention.

**(Choice C)** Hydrochlorothiazide is an antihypertensive that reduces sodium reabsorption in the distal convoluted tubule. Although beta blockers (another type of antihypertensive) are useful for migraine prevention, hydrochlorothiazide is not indicated for treatment of migraines.

**(Choice D)** Sertraline is a selective serotonin reuptake inhibitor (SSRI) used for depression and anxiety. Although tricyclic antidepressants are used for migraine prevention, SSRIs have not been shown to prevent migraines.

**Educational objective:**
Migraine is an episodic disorder characterized by severe, often unilateral headache, commonly associated with nausea and sensitivity to light and sound. Treatment is divided into abortive therapy (eg, mild analgesics, triptans, antiemetics, ergotamines) for acute symptoms and preventive therapy (eg, beta blockers, tricyclic antidepressants, anticonvulsants [topiramate, valproate]) to reduce the frequency of headaches.

| Pharmacology | Nervous System | Migraine |
|---|---|---|
| Subject | System | Topic |



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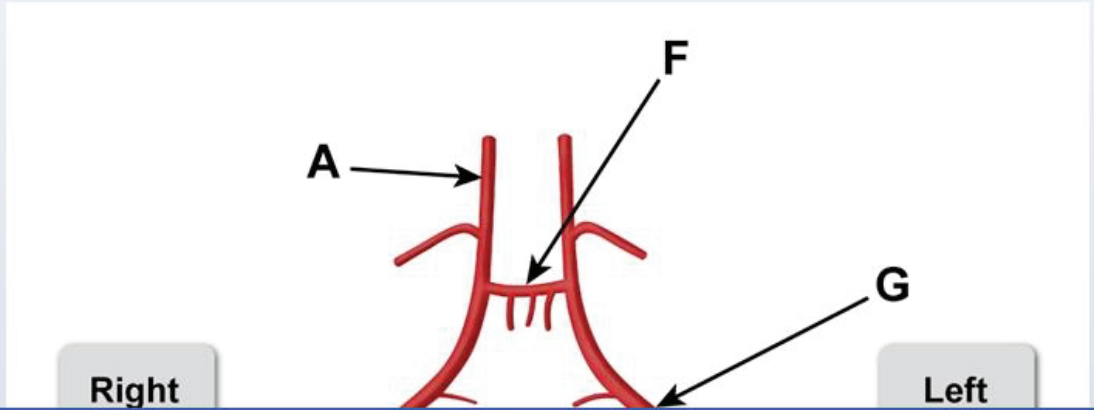
A 66-year-old, right-handed man is brought to the emergency department due to left-sided numbness and weakness. The patient woke with left-hand clumsiness that rapidly progressed to profound left-sided weakness, affecting the left arm more than the left leg. He has a history of hypertension and has smoked a pack of cigarettes daily for the past 40 years. Blood pressure is 175/90 mm Hg and pulse is 82/min and regular. Neurologic examination reveals impaired touch discrimination in the left arm with left facial weakness sparing the forehead, 2/5 muscle strength in the left upper limb, and 4/5 muscle strength in the left lower limb. Right-sided strength and visual field examinations are normal. Which of the following labeled arteries is most likely occluded in this patient?



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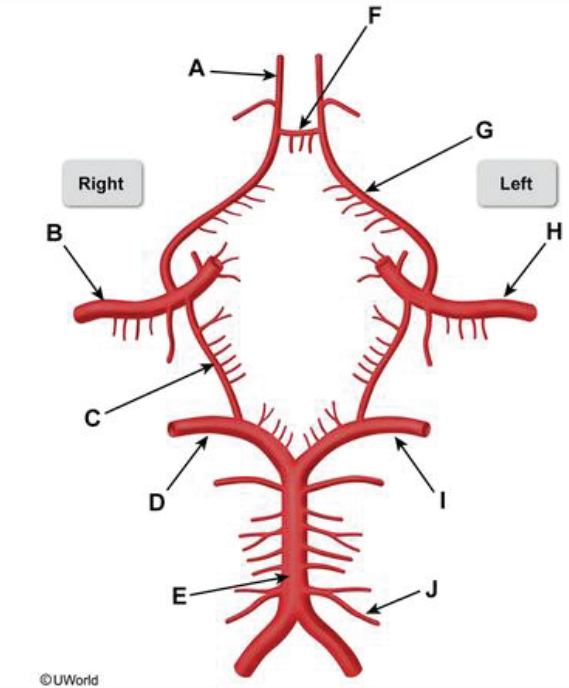


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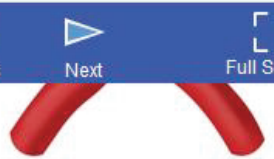

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- A. A
- B. B
- C. C
- D. D
- E. E
- F. F
- G. G
- H. H
- I. I
- J. J



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- A. A (6%)
- ✓ B. B (69%)
- C. C (4%)
- D. D (3%)
- E. E (1%)
- F. F (0%)
- G. G (2%)
- H. H (7%)
- I. I (1%)
- J. J (2%)

Correct

69%
Answered correctly

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Time Spent

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Last Updated



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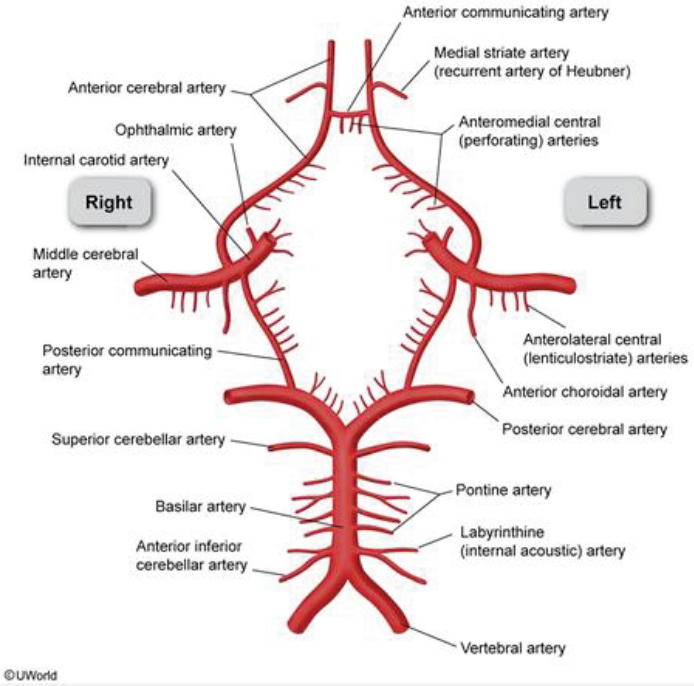


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This patient has most likely had an acute ischemic stroke involving the territory supplied by the right middle cerebral artery (MCA). Patients with **MCA occlusion** usually present with **contralateral hemiparesis** and **hemisensory loss** involving the **face and upper limb** due to infarction of the corresponding motor and sensory cortices. The contralateral lower limb is typically less affected. Other features may include spatial neglect of the contralateral side (damage to the nondominant parietal lobe) and contralateral homonymous quadrantanopia (damage to the optic radiations in the subcortical temporoparietal lobe).

If the stroke affects the dominant (usually left) hemisphere, the speech areas of the brain can be damaged. Consequently, patients with left MCA stroke (right-sided motor and sensory deficits) also often have expressive or receptive aphasia due to infarction of the Broca and Wernicke areas, respectively **(Choice H)**.

**(Choices A and G)** Occlusion of the anterior cerebral artery causes contralateral motor and sensory deficits, with the lower limb being affected more than the upper limb. Bilateral anterior cerebral artery occlusion can cause significant behavioral symptoms (eg, abulia), primitive reflexes (eg, Moro, grasp), and urinary incontinence due to damage of the prefrontal cortex.

**(Choices C and F)** Saccular aneurysms often affect the anterior and posterior communicating arteries in



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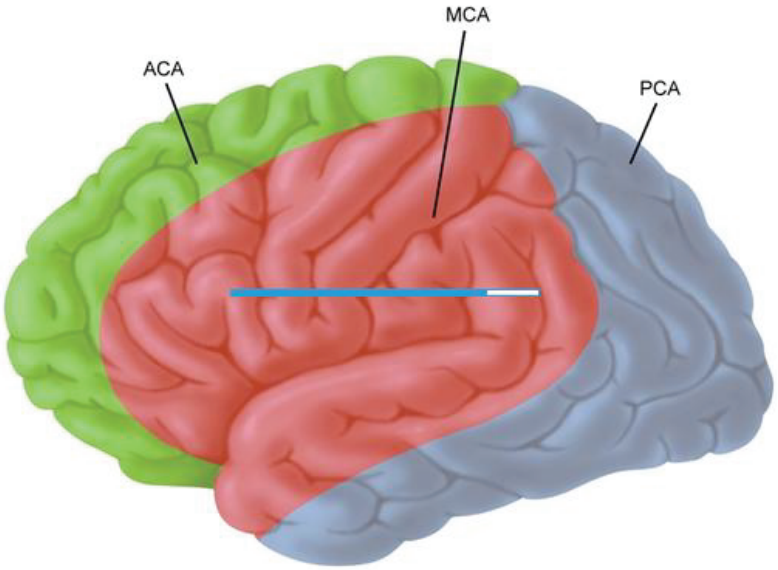
Vertebral artery

Exhibit Display

Blood supply to regions of cerebral cortex




**ACA** = anterior cerebral artery; **MCA** = middle cerebral artery; **PCA** = posterior cerebral artery.
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(Choices C and E) Saccular aneurysms often affect the anterior and posterior communicating arteries in



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Vertebral artery

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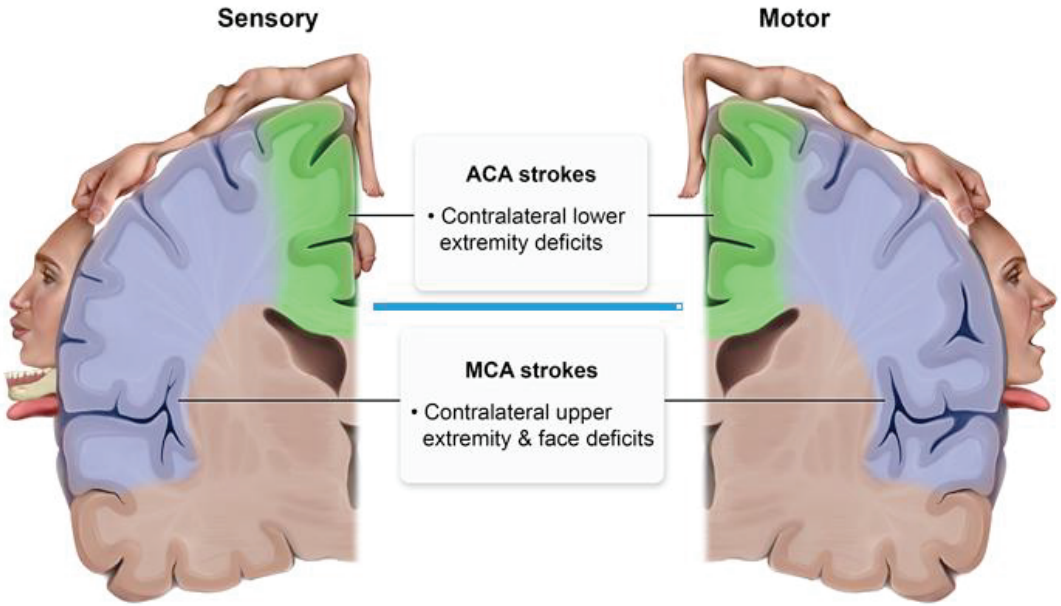
## Cerebral stroke patterns




**ACA** = anterior cerebral artery; **MCA** = middle cerebral artery.

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(Choices C and E) Saccular aneurysms often affect the anterior and posterior communicating arteries in



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Vertebral artery

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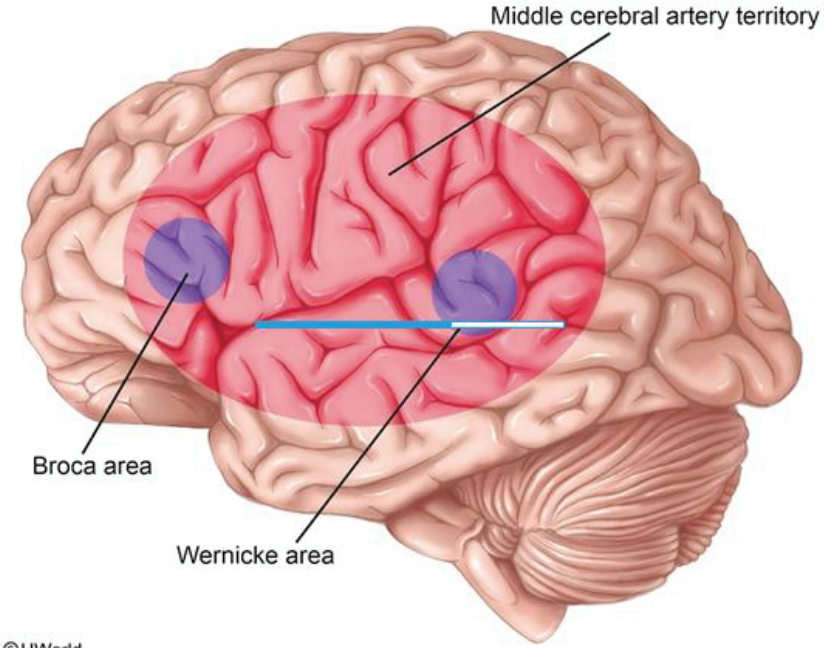
Wernicke aphasia

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(Choices C and E) Saccular aneurysms often affect the anterior and posterior communicating arteries in



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**(Choices C and F)** Saccular aneurysms often affect the anterior and posterior communicating arteries in the circle of Willis. Anterior communicating artery aneurysms can compress the central optic chiasm, causing bitemporal hemianopia. Posterior communicating artery aneurysm frequently compresses the oculomotor nerve, producing ipsilateral mydriasis, ptosis, and "down and out" eye deviation.

**(Choices D and I)** Posterior cerebral artery territory infarction typically results in contralateral hemianopia due to infarction of the visual cortex. The macula is often spared due to collateral circulation from the MCA.

**(Choice E)** Basilar artery occlusion usually damages the base of the pons, which contains the corticospinal and corticobulbar tracts, and the paramedian tegmentum. Consequently, patients typically have quadriplegia, bulbar dysfunction (eg, facial weakness, dysarthria), and oculomotor deficits (eg, horizontal gaze palsy).

**(Choice J)** Occlusion of the anterior inferior cerebellar artery causes lateral pontine syndrome. Patients with this condition typically have ipsilateral loss of pain or temperature in the face (trigeminal nucleus), ipsilateral facial weakness (facial nucleus), ipsilateral hearing impairment (cochlear nucleus), contralateral loss of pain and temperature in the trunk and extremities (lateral spinothalamic tract), and cerebellar dysfunction (eg, ataxia, dysmetria).

**Educational objective:**



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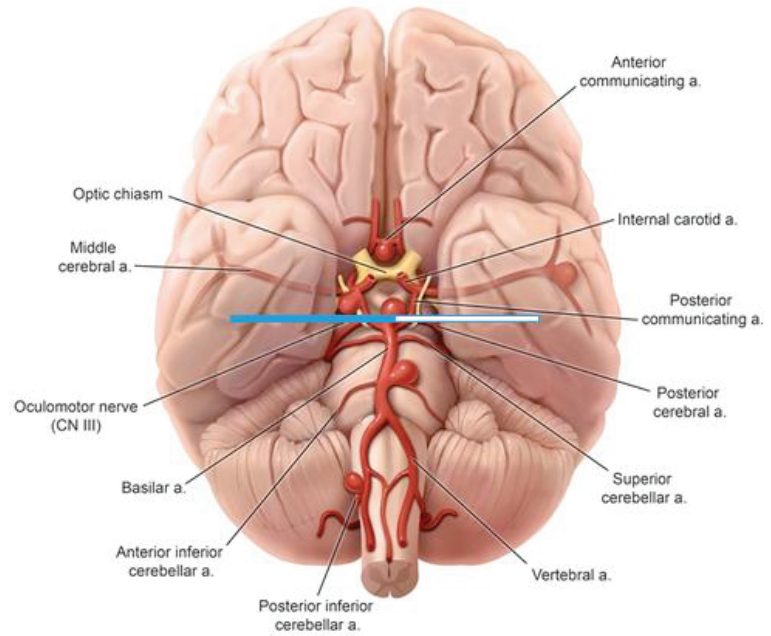
Berry (saccular) aneurysms

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**(Choice J)** Occlusion of the anterior inferior cerebellar artery causes lateral pontine syndrome. Patients with this condition typically have ipsilateral loss of pain or temperature in the face (trigeminal nucleus), ipsilateral facial weakness (facial nucleus), ipsilateral hearing impairment (cochlear nucleus), contralateral loss of pain and temperature in the trunk and extremities (lateral spinothalamic tract), and cerebellar dysfunction (eg, ataxia, dysmetria).

**Educational objective:**
Occlusion of the middle cerebral artery (MCA) typically results in contralateral hemiparesis and hemisensory loss of the face and upper limb with relative preservation of lower limb function. If the occluded MCA is in the dominant (usually left) hemisphere, aphasia may also occur.

**References**

- Stroke syndromes and clinical management.

| Anatomy | Nervous System | Ischemic stroke |
|---|---|---|
| Subject | System | Topic |



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A 42-year-old woman is hospitalized for surgical removal of a mediastinal mass. The patient has had intermittent episodes of double vision, difficulty chewing food, and weakness of the extremities for the past several months. During evaluation she was found to have a circumscribed anterior mediastinal mass. Preoperative nerve conduction studies revealed a decremental response to repetitive motor nerve stimulation. She has no other medical conditions and does not use tobacco, alcohol, or illicit drugs. The patient has no drug allergies. Compared to a healthy individual, which of the following anesthesia-related medications is most likely to have increased potency in this patient?

A. Isoflurane
B. Midazolam
C. Neostigmine
D. Atropine
E. Vecuronium

Submit



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A 42-year-old woman is hospitalized for surgical removal of a mediastinal mass. The patient has had intermittent episodes of double vision, difficulty chewing food, and weakness of the extremities for the past several months. During evaluation she was found to have a circumscribed anterior mediastinal mass. Preoperative nerve conduction studies revealed a decremental response to repetitive motor nerve stimulation. She has no other medical conditions and does not use tobacco, alcohol, or illicit drugs. The patient has no drug allergies. Compared to a healthy individual, which of the following anesthesia-related medications is most likely to have increased potency in this patient?

A. Isoflurane (7%)
B. Midazolam (2%)
C. Neostigmine (27%)
D. Atropine (16%)
E. Vecuronium (45%)

45%
01 min, 04 secs
03/15/2021



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www.ncbi.nlm.nih.gov/pubmed/24370167

This patient has an anterior mediastinal mass and a nerve conduction study consistent with **myasthenia gravis** (MG), an autoimmune disease caused by **autoantibodies** against postsynaptic **nicotinic acetylcholine receptors** of the neuromuscular junction. Antibody-induced degradation leads to fewer functional receptors, which may be insufficient to generate muscle action potentials despite normal acetylcholine release. Weakness (most commonly of the extraocular, bulbar, and proximal muscles) worsens with repetitive nerve stimulation (**fatigability**) as acetylcholine stores in the presynaptic nerve terminal are depleted. **Thymic abnormalities** (eg, thymoma, thymic hyperplasia) are common and may appear as an anterior mediastinal mass on imaging.

**Neuromuscular blocking agents** are used to induce skeletal muscle relaxation during surgery by competing with acetylcholine at the postsynaptic membrane. They can be subclassified by their effects:

- **Nondepolarizing agents** (eg, **vecuronium**, rocuronium) are **competitive antagonists** of nicotinic acetylcholine receptors. Due to the low number of functioning receptors, patients with MG are **extremely sensitive** to these agents; very small doses can induce paralysis with loss of airway patency.
- **Depolarizing agents** (eg, succinylcholine) are **competitive agonists** of nicotinic acetylcholine



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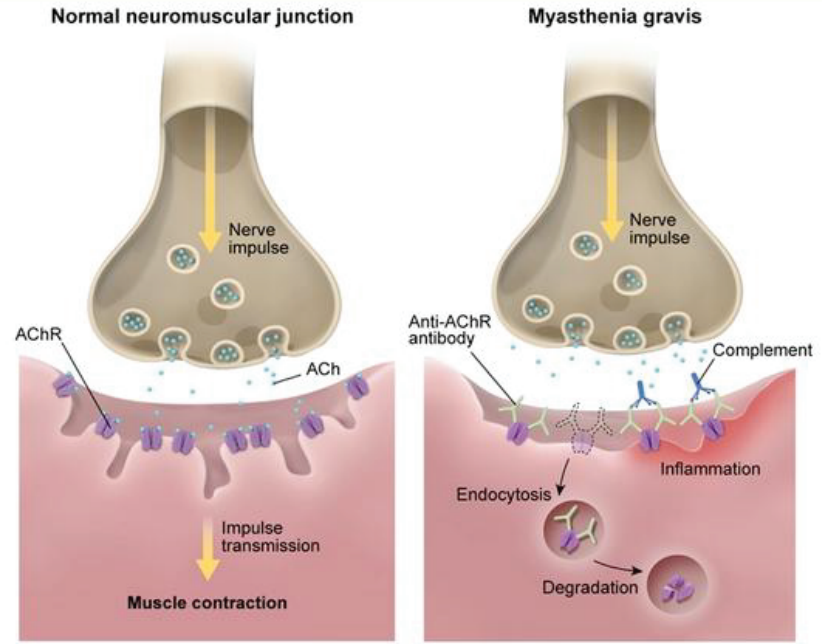


ACh = acetylcholine; AChR = acetylcholine receptor.
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patency.

- **Depolarizing agents** (eg, succinylcholine) are **competitive agonists** of nicotinic acetylcholine receptors; persistent depolarization leads to desensitization of the motor end plate. Due to the low number of functioning receptors, patients with MG are often **resistant** to these agents; extremely large doses are required to induce muscle relaxation.

**(Choices A and B)** Isoflurane is a general anesthetic (acts centrally on multiple receptors) that can cause malignant hyperthermia in those with genetic predispositions. Midazolam is a benzodiazepine (acts on the $GABA_A$ receptor) to produce sedation. These medications are not contraindicated in MG.

**(Choice C)** The mainstay of symptomatic treatment for MG is acetylcholinesterase inhibitors (eg, pyridostigmine, neostigmine); these agents inhibit the degradation of acetylcholine in the synapse, thereby increasing the amount available to stimulate muscle contractions.

**(Choice D)** Atropine is a muscarinic acetylcholine receptor antagonist often used as premedication before general anesthesia to decrease salivary and bronchial secretions (helps maintain airway patency) and prevent myocardial depression (minimizes risk of hypotension); it has no effect on nicotinic acetylcholine receptors in the neuromuscular junctions.

**Educational objective:**



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**Educational objective:**
Myasthenia gravis (MG) is caused by autoantibodies against postsynaptic nicotinic acetylcholine receptors, leading to fewer functional receptors and fatigable muscle weakness. Nondepolarizing neuromuscular blocking agents (eg, vecuronium) are competitive antagonists of nicotinic receptors; due to the depletion of receptors, patients with MG are extremely sensitive to these agents.

| Pharmacology | Nervous System | Myasthenia gravis |
|---|---|---|
| Subject | System | Topic |

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A 44-year-old woman with a history of breast cancer comes to the office due to persistent back pain. The patient was recently started on radiation treatment for several vertebral metastases. She has taken acetaminophen and nonsteroidal anti-inflammatory drugs but continues to have severe pain. On physical examination, she has tenderness over several lumbar vertebrae. Neurologic examination is unremarkable. The patient is started on oral morphine therapy. Which of the following is the most likely direct effect of this medication on the spinal cord neurons of this patient?

A. Activation of sodium-calcium exchange mechanisms
B. Blockade of voltage-dependent sodium influx
C. Increased calcium influx into the cells
D. Increased chloride influx into the cells
E. Increased potassium efflux out of the cells

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A. Activation of sodium-calcium exchange mechanisms (5%)
B. Blockade of voltage-dependent sodium influx (35%)
C. Increased calcium influx into the cells (5%)
D. Increased chloride influx into the cells (17%)
E. Increased potassium efflux out of the cells (36%)

Incorrect
Correct answer
E

36%
Answered correctly

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01/06/2021
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Correct answer
Answered correctly
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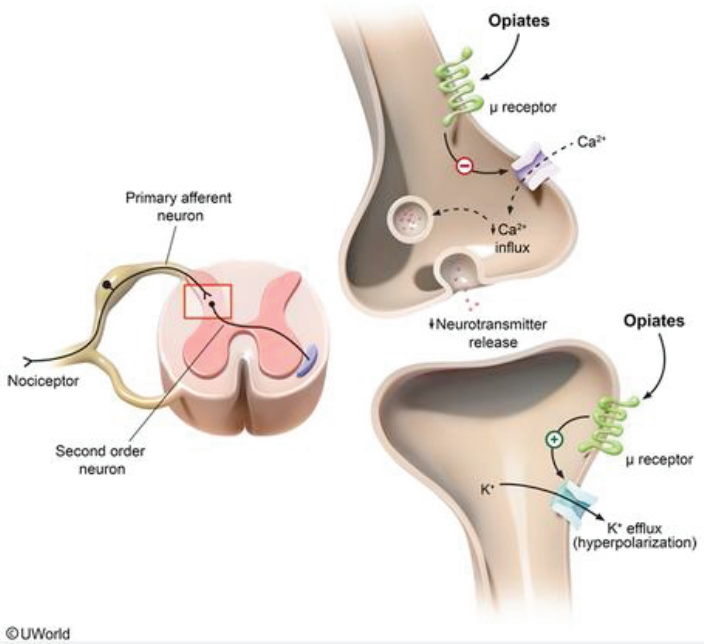
Opiate-induced analgesia

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**Morphine** is an **opiate analgesic** that is commonly used to treat severe chronic pain in patients with cancer. There are 3 main opiate receptor subtypes (eg, mu, delta, kappa) that mediate analgesia at the spinal and supraspinal levels. All of these transmembrane receptors are coupled to inhibitory G proteins. Morphine and other commonly used opiates have an especially high affinity for the **mu receptor**, which exerts the strongest analgesic effects.

In the spine, opiates bind to mu receptors on the primary afferent neuron, resulting in closure of voltage-gated calcium channels, **reduced calcium influx**, and decreased excitatory neurotransmitter release (eg, acetylcholine, norepinephrine, serotonin, glutamate, substance P) from the **presynaptic terminal (Choice C)**. Opiates also bind to mu receptors on the **postsynaptic membrane**, which opens potassium channels and leads to membrane hyperpolarization due to **potassium efflux**. Opiate-induced inhibition of synaptic activity in the central nervous system attenuates pain transmission, producing analgesia.

**(Choice A)** Digoxin is a cardiac glycoside that inhibits the sodium-potassium ATPase pump in myocardial cells, resulting in a mild increase in intracellular sodium and indirect inhibition of the sodium-calcium exchanger. This leads to increased intracellular calcium and cardiac contractility, which can help reduce symptoms in patients with advanced systolic heart failure.



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cells, resulting in a mild increase in intracellular sodium and indirect inhibition of the sodium-calcium exchanger. This leads to increased intracellular calcium and cardiac contractility, which can help reduce symptoms in patients with advanced systolic heart failure.

**(Choice B)** Local anesthetics (eg, lidocaine) reduce pain transmission by blocking voltage-dependent sodium channels, which decreases sodium influx and action potential propagation. They are typically used for minor surgical procedures and spinal anesthesia.

**(Choice D)** Benzodiazepines are sedative-hypnotics that may be indicated for anxiety, panic attacks, or insomnia. They work by increasing chloride influx at GABA-A receptors in the thalamus, limbic structures, and cerebral cortex.

**Educational objective:**

Opiate analgesics reduce pain by binding to mu receptors and inhibiting synaptic activity in the central nervous system. Activation of presynaptic mu receptors on the primary afferent neuron leads to closure of voltage-gated calcium channels and reduced excitatory neurotransmitter release. Binding to mu receptors on the postsynaptic membrane causes opening of potassium channels and membrane hyperpolarization.

**References**

- Molecular mechanisms of opioid receptor-dependent signaling and behavior.



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A 51-year-old woman comes to the physician complaining that the right side of her face has felt “funny” for the past 12 hours. Her past medical history is significant for type 2 diabetes mellitus. Physical examination reveals asymmetry of her face when she smiles, puffs out her cheeks, and closes her eyes tightly. There is also effacement of the right nasolabial fold, and her mouth is drawn toward the left side. Which of the following additional findings is most likely associated with this patient’s condition?

A. Attenuated sense of touch on the right side of face
B. Decreased tearing from the right eye
C. Failure to elevate the palate when saying “ah”
D. Inability to sweat on the right side of face
E. Loss of taste sensation from the posterior 1/3 of the tongue

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A 51-year-old woman comes to the physician complaining that the right side of her face has felt "funny" for the past 12 hours. Her past medical history is significant for type 2 diabetes mellitus. Physical examination reveals asymmetry of her face when she smiles, puffs out her cheeks, and closes her eyes tightly. There is also effacement of the right nasolabial fold, and her mouth is drawn toward the left side. Which of the following additional findings is most likely associated with this patient's condition?

A. ~~Attenuated sense of touch on the right side of face~~ (13%)
✓ B. Decreased tearing from the right eye (57%)
C. ~~Failure to elevate the palate when saying "ah"~~ (7%)
✗ D. Inability to sweat on the right side of face (14%)
E. ~~Loss of taste sensation from the posterior 1/3 of the tongue~~ (7%)

Incorrect
Correct answer
B

57%
Answered correctly

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Last Updated



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This patient's presentation is consistent with Bell's palsy, an idiopathic paresis of the facial nerve. To understand the pathophysiology of Bell's palsy, it is important to understand the function of the facial nerve (CN VII). The facial nerve is a mixed nerve, consisting of the following:

1. Motor output to the facial muscles
2. Parasympathetic innervation to the lacrimal, submandibular, and sublingual salivary glands
3. Special afferent fibers for taste from the anterior 2/3 of the tongue
4. Somatic afferents from the pinna and external auditory canal

Patients with Bell's palsy typically present with sudden onset of unilateral facial paralysis. Specific findings include impaired eye closure, eyebrow sagging, inability to smile and frown on the affected side, disappearance of the nasolabial fold, and the mouth being drawn to the non-affected side. Patients afflicted with Bell's palsy may also have decreased tearing, hyperacusis, and/or loss of taste sensation over the anterior two-thirds of the tongue.

**(Choice A)** Trigeminal nerve (CN V) somatic afferents are responsible for providing general sensation over the face; the motor branch of the trigeminal nerve ($V_3$) innervates the muscles of mastication and the tensor tympani.



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tympani.

**(Choice C)** Palate elevation and the gag reflex involve the glossopharyngeal (CN IX) and vagus (CN X) nerves.

**(Choice D)** Horner's syndrome occurs due to interruption of sympathetic innervation and clinically presents with ptosis, miosis, anhydrosis, and enophthalmos. Post-synaptic sympathetic axons travel in a perivascular plexus along the carotid arteries to reach and innervate the face.

**(Choice E)** Taste sensation from the posterior 1/3 of the tongue is provided by the glossopharyngeal nerve (CN IX).

**Educational objective:**
In addition to unilateral facial paralysis, patients with Bell's palsy may experience decreased tearing, hyperacusis, and/or loss of taste sensation over the anterior two-thirds of the tongue.

**References**

- Seventh cranial neuropathy.

| Anatomy | Nervous System | Bell's palsy |
|---|---|---|
| Subject | System | Topic |



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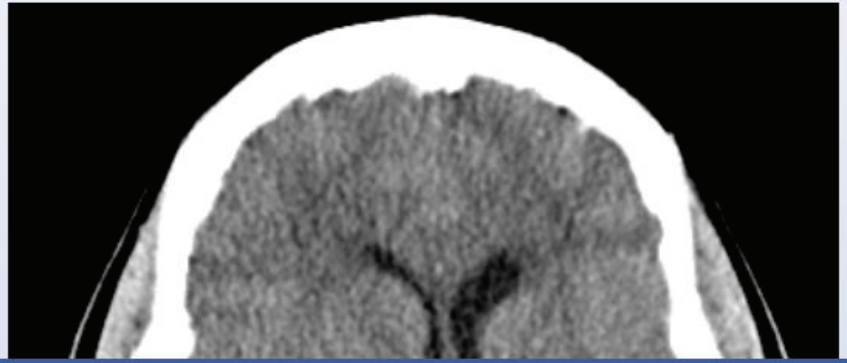
A 70-year-old right-handed woman comes to the emergency department with left-sided visual loss that she noticed on awakening in the morning. She has no headache, slurred speech, difficulty swallowing, weakness, or difficulty walking. Her other medical problems include hypertension, atrial fibrillation, and hyperlipidemia. Blood pressure is 170/102 mm Hg and pulse is 90/min and irregular. On neurologic examination, she is alert and oriented to person, place, and time. Her speech is fluent, and she follows complex commands. Examination of her visual fields shows left homonymous hemianopia with macular sparing. There is decreased sensation over the left side of her body. The remainder of the neurologic examination is within normal limits. Non-contrast head CT demonstrates an area of focal parenchymal hypoattenuation, as shown in the image below.





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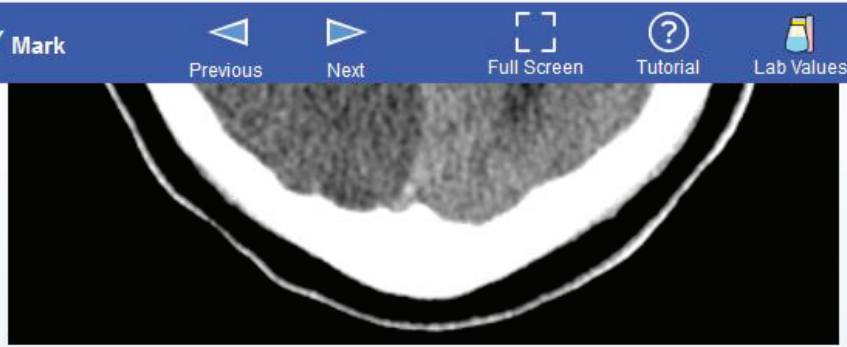

Which of the following cerebral arteries is most likely to be compromised in this patient?

A. Anterior cerebral artery
B. Anterior choroidal artery
C. Artery of Percheron
D. Basilar artery
E. Middle cerebral artery
F. Posterior cerebral artery

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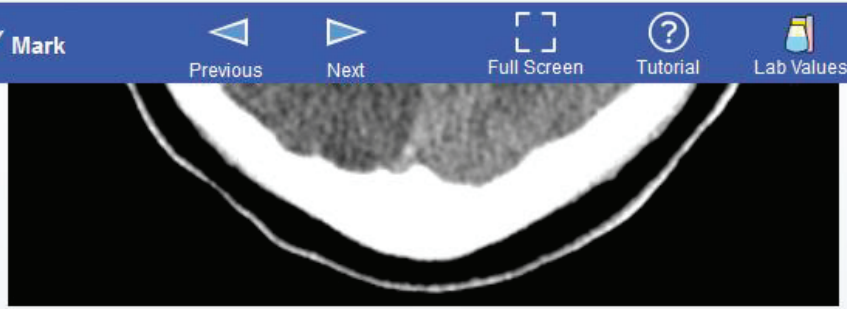

Which of the following cerebral arteries is most likely to be compromised in this patient?

A. Anterior cerebral artery (2%)
B. Anterior choroidal artery (0%)
C. Artery of Percheron (0%)
D. Basilar artery (1%)
E. Middle cerebral artery (5%)
F. Posterior cerebral artery (90%)

Correct
90%
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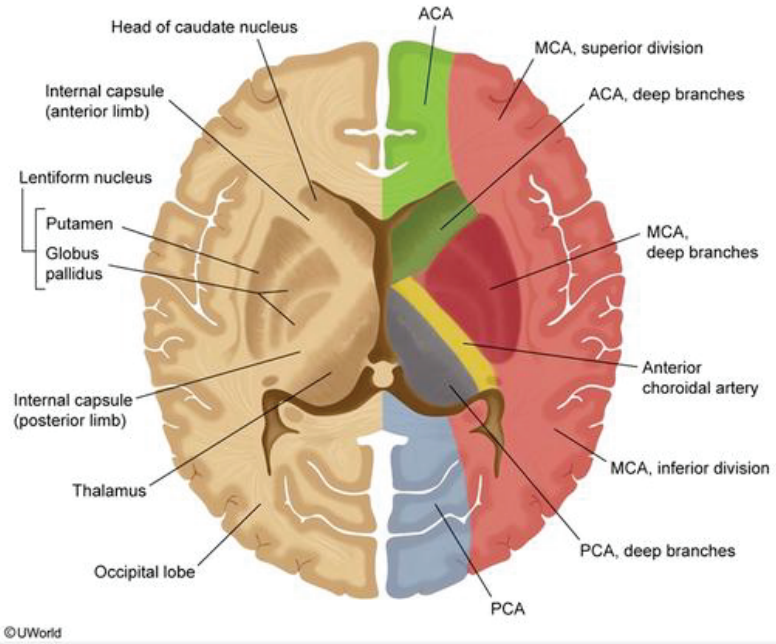
Blood supply to the cerebral hemispheres

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***(Axial images are interpreted as if viewed from the patient's feet, so the patient's right side is shown on the left side of the image.)***

This patient likely suffers from an embolic stroke due to her underlying atrial fibrillation. Non-contrast head CT demonstrates an area of focal parenchymal hypoattenuation and occipital horn effacement consistent with an evolving infarct in the distribution of the right **posterior cerebral artery** (PCA). The PCA branches off the basilar artery at the level of the pontomesencephalic junction and supplies cranial nerves III and IV and other structures in the midbrain. It also supplies the thalamus, medial temporal lobe, splenium of the corpus callosum, parahippocampal gyrus, fusiform gyrus, and occipital lobe.

The most common finding in PCA territory infarction is **contralateral hemianopia**, often with macular sparing due to collateral circulation from the middle cerebral artery. Involvement of the lateral thalamus frequently results in **contralateral paresthesias and numbness** affecting the face, trunk, and limbs. A variety of cortical symptoms can also occur, including dyslexia, visual agnosia (eg, impaired visual recognition of objects), and prosopagnosia (eg, inability to recognize faces).

**(Choice A)** The anterior cerebral artery distribution includes the inferior frontal, medial frontal, and superior medial parietal lobes; anterior 4/5 of the corpus callosum; olfactory bulb and tract; anterior portions of the basal ganglia; and internal capsule.



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**Axial images are interpreted as if viewed from the patient's feet, so the patient's right side is

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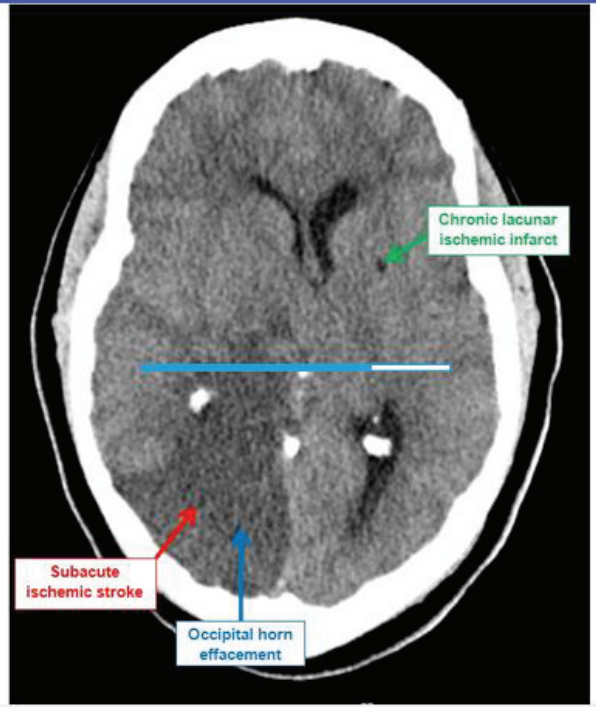


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basal ganglia, and internal capsule.

**(Choice B)** The anterior choroidal artery is the last branch off the internal carotid artery before it trifurcates. It supplies the posterior limb of the internal capsule, optic tract, lateral geniculate body, choroid plexus, uncus, hippocampus, and amygdala.

**(Choice C)** The artery of Percheron branches off either the right or left PCA and supplies the bilateral thalami and dorsal midbrain. It is considered to be a rare normal variant and can be seen in patients with bilateral thalamic or dorsal midbrain strokes.

**(Choice D)** The basilar artery supplies a large portion of the brain, including most of the brainstem and bilateral cerebellar hemispheres.

**(Choice E)** The middle cerebral artery distribution includes the lateral convexity of the frontal, parietal, and temporal lobes. It also supplies deep subcortical structures, such as the internal capsule and basal ganglia. Ischemic stroke occurs most frequently within this region, causing contralateral motor and sensory deficits involving the upper and lower extremities and face.

**Educational objective:**
The posterior cerebral artery branches off the basilar artery and supplies cranial nerves III and IV and other structures in the midbrain. It also supplies the thalamus, medial temporal lobe, splenium of the corpus


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basal ganglia, and internal capsule.

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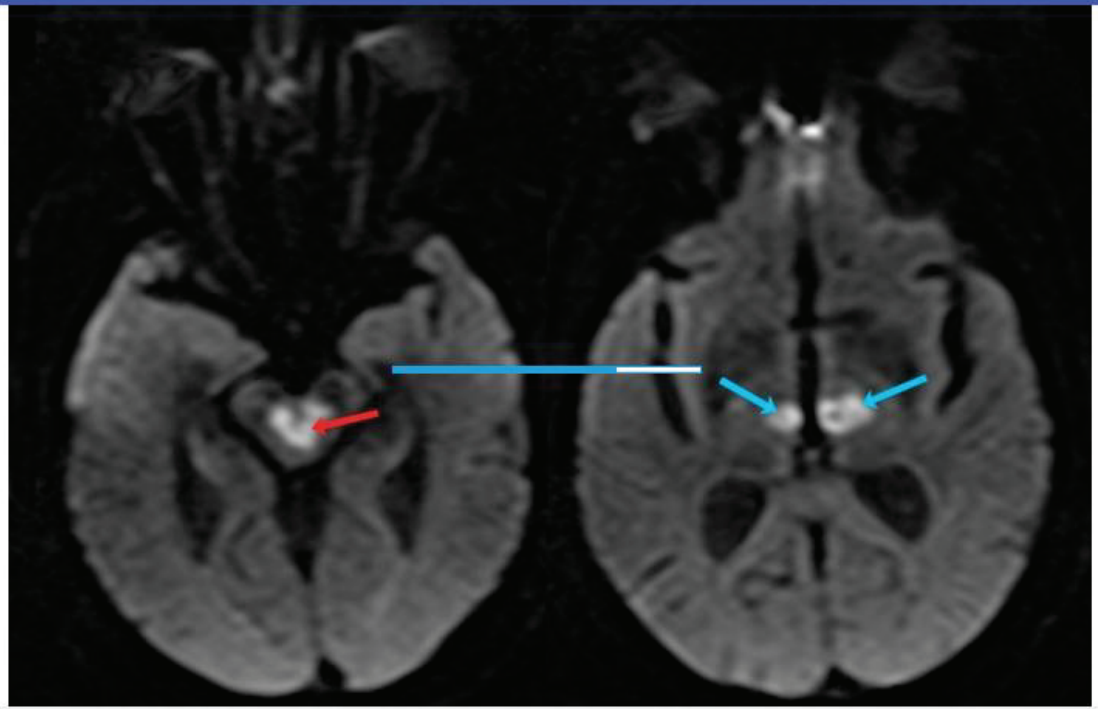

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basal ganglia, and internal capsule.

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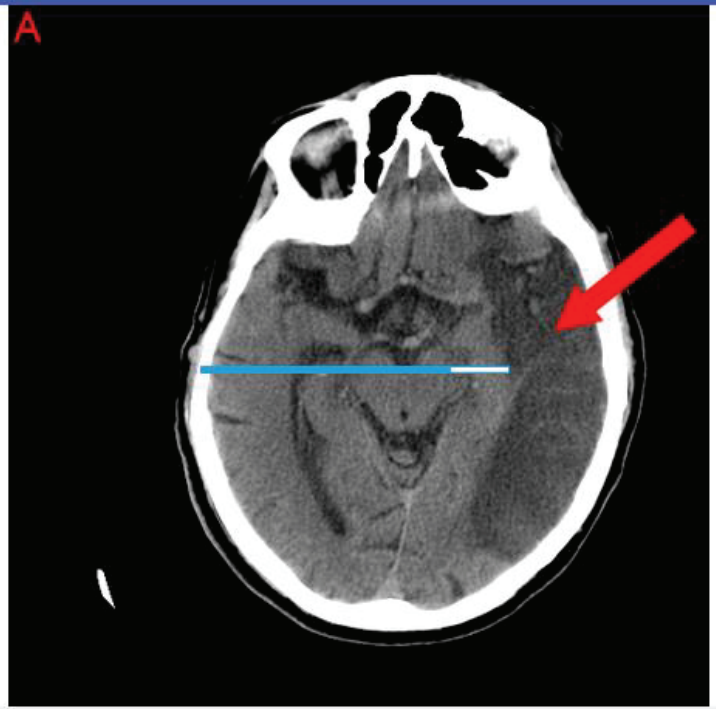


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**Educational objective:**

The posterior cerebral artery branches off the basilar artery and supplies cranial nerves III and IV and other structures in the midbrain. It also supplies the thalamus, medial temporal lobe, splenium of the corpus callosum, and occipital lobe. The most common finding with posterior cerebral artery stroke is contralateral homonymous hemianopia, often with macular sparing.

**References**

- Ischemic posterior circulation stroke: a review of anatomy, clinical presentations, diagnosis, and current management.



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A 62-year-old hospitalized woman is evaluated for muscle weakness. The patient was admitted 2 weeks ago due to septic shock from acute pyelonephritis. She was treated in the intensive care unit with intravenous fluids, vasopressors, and broad-spectrum antibiotics. The patient was also mechanically ventilated due to respiratory failure. Her hemodynamic status and infection gradually improved, but she has had difficulty being taken off the ventilator due to respiratory muscle weakness. She is also noted to have significant extremity weakness. Physical examination shows diffuse mild atrophy of the extremity muscles. Bilateral upper and lower extremity deep tendon reflexes are decreased. Which of the following is the most likely cause of this patient's current condition?

A. Corticospinal tract demyelination
B. Motor cortex ischemic injury
C. Motor endplate receptor loss
D. Myofiber lymphocytic inflammation
E. Peripheral nerve axonal degeneration



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- A. Corticospinal tract demyelination (16%)
- B. ~~Motor cortex ischemic injury~~ (12%)
- C. ~~Motor endplate receptor loss~~ (19%)
- D. ~~Myofiber lymphocytic inflammation~~ (9%)
- E. Peripheral nerve axonal degeneration (41%)

Incorrect
Correct answer

41%

02 mins, 39 secs

01/31/2021



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This patient has weakness, muscle atrophy, and decreased deep tendon reflexes after **critical illness**. Critical illness, especially due to sepsis, can result in **neuromuscular weakness** caused by one or both of the following:

- Critical illness myopathy (CIM), which results in a decrease of muscle membrane excitability and loss of myosin with resultant **atrophy of myofibers**
- Critical illness polyneuropathy (CIP), which results in decreased nerve excitability (due to inactivation of sodium channels) and **axonal degeneration** (possibly due to injury to the microcirculation by inflammatory mediators)

Clinical features of CIM and CIP typically include symmetric weakness greater in **proximal**, rather than distal, muscles with **decreased deep tendon reflexes**. It is often diagnosed when patients are unable to be liberated from the ventilator due to chest wall weakness. Treatment is focused on controlling underlying medical conditions, preventing further complications, and rehabilitation. Patients may improve over weeks to months with rehabilitation, but many have persistent weakness.

**(Choice A)** Corticospinal tract demyelination can occur at multiple levels including the pons (eg, central pontine myelinolysis) or spinal cord (eg, vitamin $B_{12}$ deficiency). However, this would result in upper motor neuron signs (eg, hyperreflexia)



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**(Choice A)** Corticospinal tract demyelination can occur at multiple levels including the pons (eg, central pontine myelinolysis) or spinal cord (eg, vitamin $B_{12}$ deficiency). However, this would result in upper motor neuron signs (eg, hyperreflexia).

**(Choice B)** Patients with sepsis have an increased risk of stroke, which can result in motor cortex ischemic injury. However, patients with stroke often have asymmetric neurologic findings, and because it affects upper motor neurons, hyperreflexia (rather than loss of deep tendon reflexes) would be expected.

**(Choice C)** Myasthenia gravis (MG) can lead to antibody-induced motor endplate receptor loss; myasthenic crisis can be triggered by infection and lead to respiratory failure. However, patients with MG rarely have muscle atrophy, and deep tendon reflexes are classically preserved (MG causes fatigable weakness).

**(Choice D)** Myofiber lymphocytic inflammation occurs with inflammatory myopathies (eg, polymyositis), which classically present insidiously (rather than over 2 weeks) with symmetrical proximal muscle weakness. In addition, polymyositis does not typically affect the respiratory muscles, and deep tendon reflexes are usually normal.

**Educational objective:**

Critical illness can lead to weakness due to both myopathy (eg, atrophy of muscles) and polyneuropathy



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affects upper motor neurons; hyperreflexia (rather than loss of deep tendon reflexes) would be expected.

**(Choice C)** Myasthenia gravis (MG) can lead to antibody-induced motor endplate receptor loss; myasthenic crisis can be triggered by infection and lead to respiratory failure. However, patients with MG rarely have muscle atrophy, and deep tendon reflexes are classically preserved (MG causes fatigable weakness).

**(Choice D)** Myofiber lymphocytic inflammation occurs with inflammatory myopathies (eg, polymyositis), which classically present insidiously (rather than over 2 weeks) with symmetrical proximal muscle weakness. In addition, polymyositis does not typically affect the respiratory muscles, and deep tendon reflexes are usually normal.

**Educational objective:**
Critical illness can lead to weakness due to both myopathy (eg, atrophy of muscles) and polyneuropathy (eg, axonal degeneration, decreased nerve excitability). This can lead to both extremity weakness and difficulty breathing due to chest wall weakness.

| Pathophysiology | Nervous System | Critical illness polyneuromyopathy |
|---|---|---|
| Subject | System | Topic |

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A 61-year-old woman comes to the clinic due to vision problems for the last 6 months. The patient says her eyes get tired easily, especially in the late afternoon and evening. She has smoked a pack of cigarettes daily for the past 35 years and does not use alcohol or illicit drugs. On physical examination, there is weakness of the extraocular muscles. Pupillary reflex, deep tendon reflexes, and sensation are normal. A contrast-enhanced CT scan of the chest is shown in the exhibit. Which of the following is the most likely mechanism underlying this patient's symptoms?

A. Antibodies against a neurotransmitter receptor
B. Antibodies against a presynaptic calcium channel
C. $CD8^+$ lymphocyte–mediated nerve fiber demyelination
D. $CD8^+$ lymphocyte–mediated skeletal muscle damage
E. Vascular deposition of circulating immune complexes

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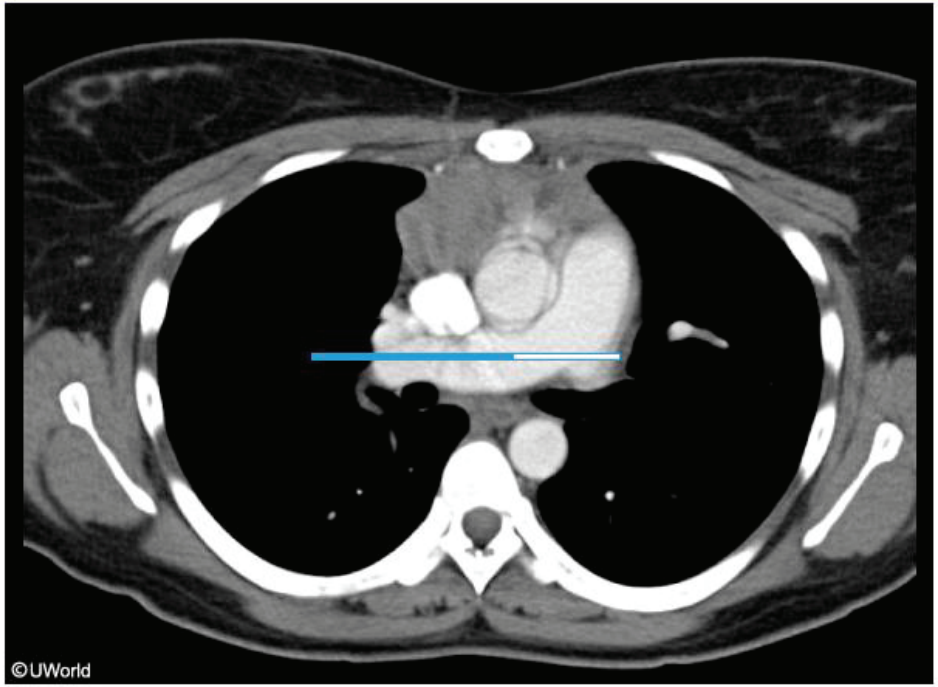


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- ✓ A. Antibodies against a neurotransmitter receptor (71%)
- B. Antibodies against a presynaptic calcium channel (18%)
- C. $CD8^+$ lymphocyte–mediated nerve fiber demyelination (3%)
- D. $CD8^+$ lymphocyte–mediated skeletal muscle damage (1%)
- E. Vascular deposition of circulating immune complexes (4%)

Correct

71%
Answered correctly

01 min, 12 secs
Time Spent

12/22/2020
Last Updated



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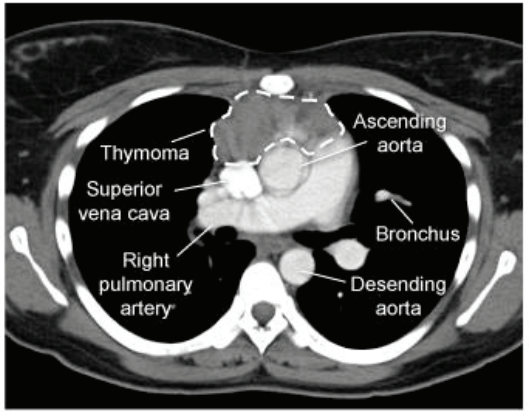
**Thymoma**




Normal

Anterior mediastinal mass

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This patient's presentation is consistent with **myasthenia gravis** (MG), an autoimmune disease caused by **autoantibodies** directed against **nicotinic acetylcholine receptors** on the postsynaptic membrane of the neuromuscular junction. Acetylcholine binding normally opens these ligand-gated sodium channels, and the subsequent influx of sodium ions raises endplate potential. To produce a self-propagating muscle action potential, there must be enough activated acetylcholine receptors to allow the endplate potential to reach threshold. In MG, antibody binding leads to receptor degradation and complement-mediated



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reach threshold. In MG, antibody binding leads to receptor degradation and complement-mediated damage of the postsynaptic membrane, preventing action potentials from being triggered.

Patients commonly have **fluctuating weakness** that worsens throughout the day and most often involves the **extraocular** (eg, ptosis, diplopia) and bulbar (eg, fatigable chewing, dysphagia) muscles. Ptosis can increase when the patient sustains an upward gaze, and electrophysiologic studies may demonstrate decreasing force of muscle contraction with repetitive stimulation. Most patients have thymic abnormalities (eg, **thymoma**, thymic hyperplasia) that may appear as an **anterior mediastinal mass** on chest imaging.

**(Choice B)** Lambert-Eaton syndrome is caused by autoantibodies directed against the presynaptic calcium channel, which causes reduced acetylcholine release. Patients usually have proximal extremity weakness that improves with muscle use, as opposed to the fatigable weakness of extraocular and bulbar muscles common in MG. In addition, hyporeflexia (vs normal reflexes) is typically present.

**(Choice C)** Guillain-Barré syndrome is caused by segmental demyelination of peripheral nerves by infiltrating T lymphocytes ($CD8^+$) and autoantibody formation. Patients with this acute inflammatory polyneuropathy can have ocular muscle weakness; however, symmetric ascending muscle weakness is classic, and symptoms typically progress rapidly over hours to days (vs months).

**(Choice D)** Polymyositis is an autoimmune disease that occurs due to $CD8^+$ lymphocyte–mediated skeletal


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reach threshold. In MG, antibody binding leads to receptor degradation and complement-mediated

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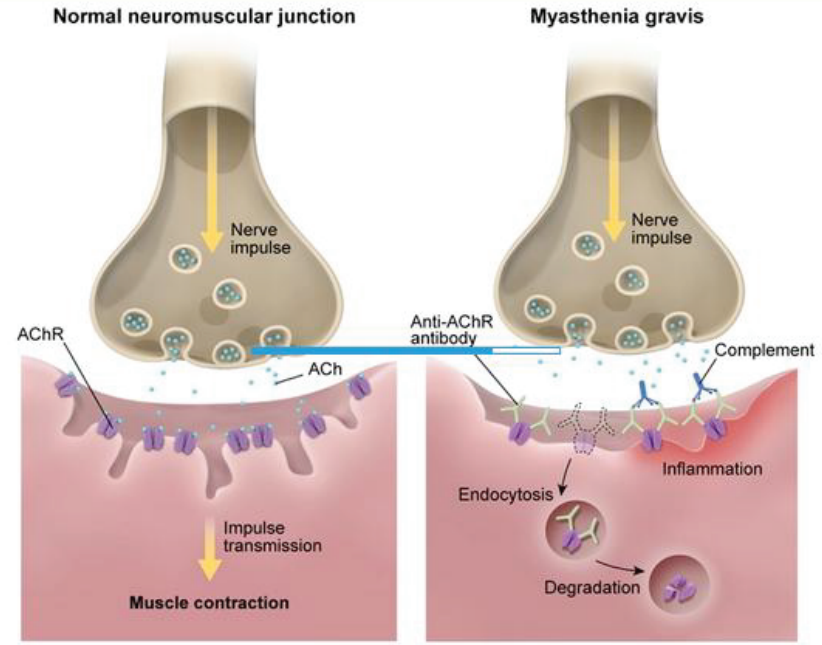


ACh = acetylcholine; AChR = acetylcholine receptor.
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classic, and symptoms typically progress rapidly over hours to days (vs months).

**(Choice D)** Polymyositis is an autoimmune disease that occurs due to $CD8^+$ lymphocyte–mediated skeletal muscle damage. It usually presents with symmetric proximal muscle weakness (eg, hip flexors) rather than extraocular muscle weakness.

**(Choice E)** Vascular deposition of circulating immune complexes—as may occur in connective tissue disorders such as systemic lupus erythematosus and rheumatoid arthritis—can cause inflammation of blood vessel walls (vasculitis) and a wide range of symptoms. Muscle weakness can occur but is unlikely to be isolated to extraocular muscles or fluctuate over the course of the day.

**Educational objective:**

Myasthenia gravis is caused by circulating antibodies directed against acetylcholine receptors of the neuromuscular junction. Autoantibody binding leads to receptor degradation, producing fluctuating weakness that worsens throughout the day and most commonly affects the extraocular muscles (eg, ptosis, diplopia). Most patients have thymic abnormalities (eg, thymoma).

**References**

- Myasthenia gravis: a review.



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A 44-year-old man with a history of advanced HIV is brought to the office by his family due to progressive cognitive decline. Over the last several years he has had worsening memory deficits and difficulty carrying out simple mental tasks. The patient has had no headaches, slurred speech, muscle weakness, or changes in vision. He was diagnosed with HIV 7 years ago, but his medical follow-up and treatment compliance have been poor. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. He has difficulty with delayed recall as well as several executive function tasks. The remainder of his neurologic examination is unremarkable. Two weeks later, he dies from severe pneumonia and respiratory failure. Which of the following histopathologic findings would most likely be found on biopsy of this patient's brain?

A. Amyloid deposits in the cortical blood vessels
B. Congo red staining plaques in the hippocampus
C. Eosinophilic, round, cytoplasmic neuronal inclusions
D. Microglial nodules and multinucleated giant cells
E. Profound neuronal loss in the caudate nucleus


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A. Amyloid deposits in the cortical blood vessels
B. Congo red staining plaques in the hippocampus
C. Eosinophilic, round, cytoplasmic neuronal inclusions
D. Microglial nodules and multinucleated giant cells
E. Profound neuronal loss in the caudate nucleus
F. Slit-like white matter cavities with surrounding gliosis


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changes in vision. He was diagnosed with HIV 7 years ago, but his medical follow-up and treatment compliance have been poor. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. He has difficulty with delayed recall as well as several executive function tasks. The remainder of his neurologic examination is unremarkable. Two weeks later, he dies from severe pneumonia and respiratory failure. Which of the following histopathologic findings would most likely be found on biopsy of this patient's brain?

A. Amyloid deposits in the cortical blood vessels (5%)

✗ B. Congo red staining plaques in the hippocampus (16%)

C. ~~Eosinophilic, round, cytoplasmic neuronal inclusions~~ (17%)

✓ D. Microglial nodules and multinucleated giant cells (42%)

E. ~~Profound neuronal loss in the caudate nucleus~~ (3%)

F. ~~Slit-like white matter cavities with surrounding gliosis~~ (15%)

Incorrect
Correct answer

42%

02 mins, 05 secs

12/09/2020



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This patient with a history of long-standing HIV infection, medical noncompliance, and progressive cognitive decline likely had **HIV-associated dementia**. Most cases occur in those with advanced HIV who have CD4 counts <200/mm$^3$. Patients usually develop features of **subcortical** dementia, including attention or working memory deficits, executive dysfunction, and slow information processing.

HIV enters the central nervous system via infected monocytes and establishes a productive infection in **microglial cells** (resident macrophages of the central nervous system) and blood-derived perivascular macrophages. Activation of these cells occurs in response to the infection, inflammatory cytokines, and HIV-derived proteins, which leads them to cluster around small areas of necrosis (forming **microglial nodules**) and fuse together to form **multinucleated giant cells**. Because HIV does not directly infect neurons, the underlying pathology of HIV-associated dementia is thought to stem from the **release of neurotoxic compounds** by these activated monocytes.

**(Choices A and B)** Cerebral amyloid angiopathy is marked by beta-amyloid deposits in the walls of cortical blood vessels. This condition is usually asymptomatic but can be associated with intracerebral hemorrhage or Alzheimer dementia. Alzheimer dementia is also associated with neuritic (senile) plaques, which are extracellular deposits of beta-amyloid surrounded by dystrophic neurites; they stain positive with Congo red and are often located in the hippocampus. Alzheimer dementia is typically seen in older adults


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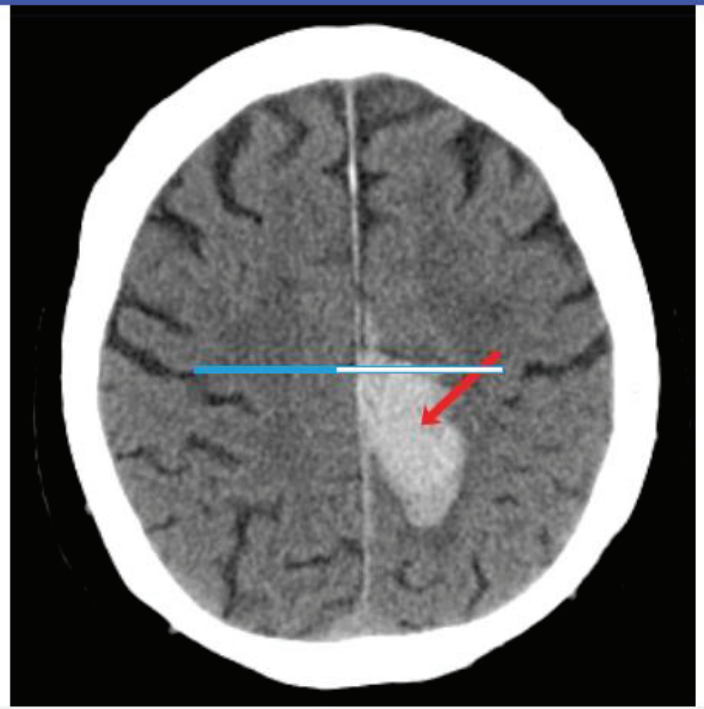

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hemorrhage or Alzheimer dementia. Alzheimer dementia is also associated with neuritic (senile) plaques, which are extracellular deposits of beta-amyloid surrounded by dystrophic neurites; they stain positive with Congo red and are often located in the hippocampus. Alzheimer dementia is typically seen in older adults and is characterized by slowly progressive memory impairment and higher cortical dysfunction (eg, aphasia, agnosia, apraxia).

**(Choice C)** Patients with rabies develop eosinophilic inclusion bodies in the cytoplasm of neuronal cells (Negri bodies). Rabies is a neurotropic virus that is transmitted by the saliva of infected animals, usually via a bite wound. Patients classically develop fever, hydrophobia (fear of water), and pharyngeal spasms.

**(Choice E)** Huntington disease is an autosomal dominant disorder that causes choreiform movement, psychiatric disturbances, and dementia. It is characterized by severe neuronal loss in the caudate nucleus.

**(Choice F)** Lacunar infarctions cause slit-like white matter cavities with surrounding gliosis. Recurrent lacunar infarctions can result in vascular dementia, which is often characterized by sudden/stepwise cognitive decline and focal neurologic deficits. Patients with vascular dementia are typically older and usually have cardiovascular risk factors.

**Educational objective:**

HIV-associated dementia should be suspected in patients with AIDS who have progressive cognitive



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aphasia, agnosia, apraxia).

**(Choice C)** Patients with rabies develop eosinophilic inclusion bodies in the cytoplasm of neuronal cells (Negri bodies). Rabies is a neurotropic virus that is transmitted by the saliva of infected animals, usually via a bite wound. Patients classically develop fever, hydrophobia (fear of water), and pharyngeal spasms.

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**(Choice F)** Lacunar infarctions cause slit-like white matter cavities with surrounding gliosis. Recurrent lacunar infarctions can result in vascular dementia, which is often characterized by sudden/stepwise cognitive decline and focal neurologic deficits. Patients with vascular dementia are typically older and usually have cardiovascular risk factors.

**Educational objective:**

HIV-associated dementia should be suspected in patients with AIDS who have progressive cognitive decline. The characteristic histopathologic finding is microglial nodules (groups of activated microglia/macrophages around small areas of necrosis) and multinucleated giant cells.

**References**

- Etiology of microglial nodules in brains of patients with acquired immunodeficiency syndrome.



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A researcher conducts a study to evaluate the morphological changes of various cerebral pathologies using live animal models. In an experiment, histopathological examination of the brain after an inciting event shows neurons with intensely eosinophilic cytoplasm and condensed basophilic nuclei. Serial biopsies are obtained to evaluate progressive changes. Which of the following is most likely to be seen in the affected brain area in the subsequent weeks?

A. Extracellular amyloid deposition
B. Fibroblast migration
C. Glial cell hyperplasia
D. Neuronal hypertrophy
E. Vascular hyalinization

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A researcher conducts a study to evaluate the morphological changes of various cerebral pathologies using live animal models. In an experiment, histopathological examination of the brain after an inciting event shows neurons with intensely eosinophilic cytoplasm and condensed basophilic nuclei. Serial biopsies are obtained to evaluate progressive changes. Which of the following is most likely to be seen in the affected brain area in the subsequent weeks?

A. Extracellular amyloid deposition (6%)
B. Fibroblast migration (15%)
C. Glial cell hyperplasia (71%)
D. Neuronal hypertrophy (3%)
E. Vascular hyalinization (3%)

Correct

71%
Answered correctly

34 secs
Time Spent

02/23/2021
Last Updated



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| Type of glial cell | Origin | Appearance | Functions |
|---|---|---|---|
| **Astrocytes** | Neuroectoderm | • Round vesicular nuclei<br>• Contain glial fibrils, composed of glial fibrillary acidic protein | • Repair<br>• Structural & metabolic support<br>• Blood-brain barrier |
| **Oligodendrocytes** | Neuroectoderm | • Small nuclei surrounded by a pale halo | • Production of |



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| | | | |
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| | | protein | |
| **Oligodendrocytes** | Neuroectoderm | • Small nuclei surrounded by a pale halo<br>• Fewer processes than astrocytes | • Production of myelin |
| **Microglia** | Primitive yolk sac macrophages | • Small elongated nuclei<br>• Many short branching processes | • Phagocytosis |

The histopathological findings of neurons with shrunken, basophilic nuclei and intensely eosinophilic cytoplasm (**red neurons**) are indicative of **irreversible neuronal damage**. In response to irreversible


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| | | | |
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| | | processes | |

The histopathological findings of neurons with shrunken, basophilic nuclei and intensely eosinophilic cytoplasm (**red neurons**) are indicative of **irreversible neuronal damage**. In response to irreversible injury and neuronal death, astrocytes proliferate at the site of injury to restore tissue integrity (a role analogous to fibroblasts outside the CNS). This process is called astrocytosis (or **gliosis**) and is a universal response of the CNS to severe damage. As astrocytes proliferate, they replace lost neurons, compensate for their volume, and over time form a closely connected, firm meshwork called a **gliotic scar**.

**(Choices A and E)** Although both vascular hyalinization and amyloid deposition can lead to neural injury, both would show accumulations of *extracellular* eosinophilic material on histopathological examination.

**(Choice B)** Fibroblast migration to a site of injury occurs in most of the peripheral tissues of the body, but not the CNS, where tissue repair is a function of astrocytes.

**(Choice D)** Irreversibly injured neurons do not hypertrophy; they undergo cellular necrosis. Microglia are responsible for phagocytizing the resulting dead cells and debris.

**Educational objective:**
CNS injury is associated with astrocyte hypertrophy and proliferation (gliosis). This process leads to the formation of a glial scar, which compensates for the volume loss that occurs after neuronal death.


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processes

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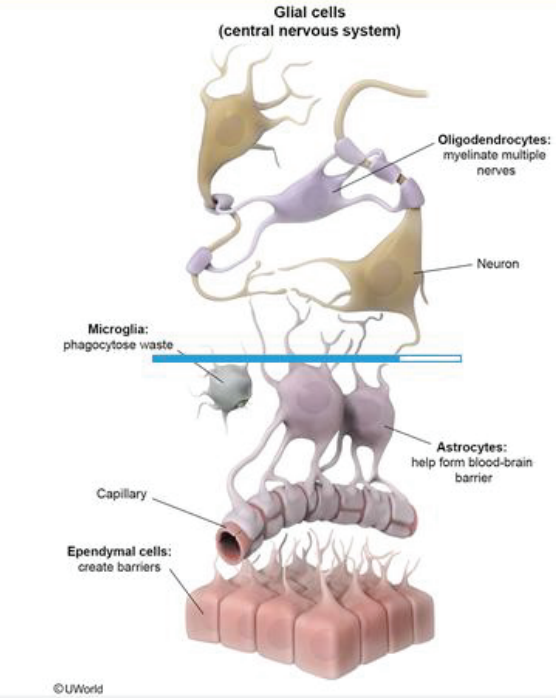


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formation of a glial scar, which compensates for the volume loss that occurs after neuronal death.



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processes

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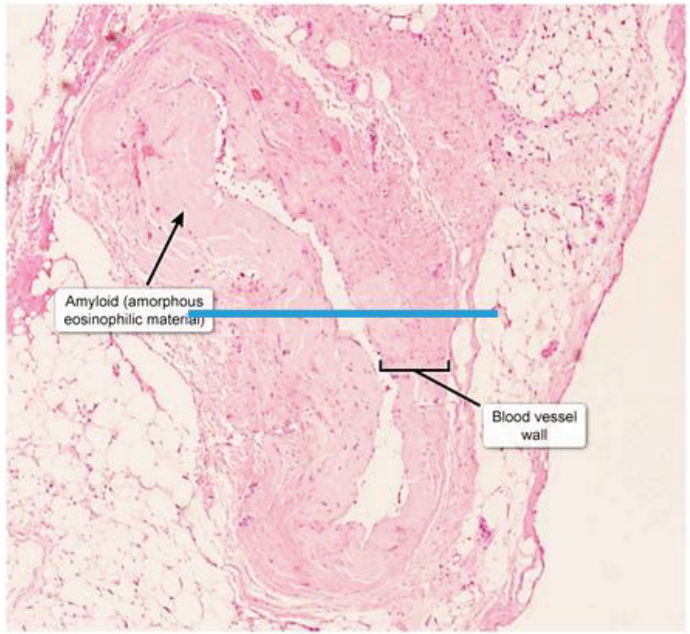
Amyloidosis

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analogous to fibroblasts outside the CNS). This process is called astrocytosis (or **gliosis**) and is a universal response of the CNS to severe damage. As astrocytes proliferate, they replace lost neurons, compensate for their volume, and over time form a closely connected, firm meshwork called a **gliotic scar**.

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**Educational objective:**
CNS injury is associated with astrocyte hypertrophy and proliferation (gliosis). This process leads to the formation of a glial scar, which compensates for the volume loss that occurs after neuronal death.

| Pathology | Nervous System | Ischemic stroke |
|---|---|---|
| Subject | System | Topic |

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A 42-year-old woman comes to the office with her husband for evaluation of abnormal movements. The patient has been having involuntary facial grimaces and extremity fidgeting. She has no prior medical or psychiatric conditions, but her husband says she has had frequent anger outbursts over the past year. The patient takes no medications. She smoked cigarettes and used illicit drugs for several years during college but not since then. Her father died of a neurological disorder at age 55. Physical examination shows intermittent, fidgety, jerky movements of the hands. MRI of the brain is ordered. Which of the following neuroimaging findings is most likely to be seen in this patient?

A. Diffuse ventriculomegaly without sulcal widening
B. Enlargement of frontal horns of the lateral ventricles
C. Hypoplastic vermis with a dilated fourth ventricle
D. Pronounced atrophy of bilateral hippocampi
E. Regional atrophy of frontal and temporal lobes

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A. Diffuse ventriculomegaly without sulcal widening (16%)
B. Enlargement of frontal horns of the lateral ventricles (44%)
C. Hypoplastic vermis with a dilated fourth ventricle (3%)
D. Pronounced atrophy of bilateral hippocampi (9%)
E. Regional atrophy of frontal and temporal lobes (25%)

44%
01 min, 22 secs
09/28/2020



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| Huntington disease features | |
|---|---|
| **Pathogenesis** | • Autosomal dominant inheritance<br>• Increased number of CAG repeats in *HTT* gene<br>• Anticipation: earlier onset, more severe disease in subsequent generations<br>• Gain of function mutation: protein accumulation toxic to neurons<br>• Decrease in GABA and acetylcholine in caudate nuclei |
| **Clinical features** | • Chorea: involuntary, jerky movements of face and extremities<br>• Behavioral abnormalities (eg, aggressiveness, depression)<br>• Progressive dementia |
| **Confirmatory testing** | • Neuroimaging: caudate atrophy with enlargement of the lateral ventricles<br>• Genetic testing for # of CAG repeats |

This patient with chorea (eg, fidgety, jerky, involuntary movements), behavioral abnormalities (eg, outbursts of anger), and a family history of a fatal neurological disease likely has **Huntington disease** (HD). HD is


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This patient with chorea (eg, fidgety, jerky, involuntary movements), behavioral abnormalities (eg, outbursts of anger), and a family history of a fatal neurological disease likely has **Huntington disease** (HD). HD is an autosomal dominant, progressive neurodegenerative disorder that results in the production and accumulation of abnormal huntingtin protein, which is toxic to neurons.

Although patients with HD display generalized cortical **atrophy** as the disease progresses, the most prominent atrophy is seen bilaterally in the **caudate nucleus** and putamen, leading to the **enlargement** of the frontal horns of the **lateral ventricles**. The loss of inhibitory GABAergic neurons in these areas causes decreased regulation of the movement and behavioral centers of the cerebral cortex, resulting in the characteristic constellation of symptoms in patients with HD.

**(Choice A)** Diffuse ventriculomegaly *without sulcal widening* is seen in normal pressure hydrocephalus (eg, urinary incontinence, gait disturbance, cognitive impairment) due to an increase in cerebrospinal fluid volume. In contrast, neurodegenerative disorders such as Huntington disease typically present with both ventriculomegaly and sulcal widening due to generalized cortical atrophy.

**(Choice C)** A hypoplastic cerebellar vermis with cystic dilation of the fourth ventricle and a posterior fossa cyst is characteristic of congenital Dandy-Walker malformation. Although the diagnosis of Dandy-Walker malformation can be delayed into early adulthood, patients typically have a long history of chronic


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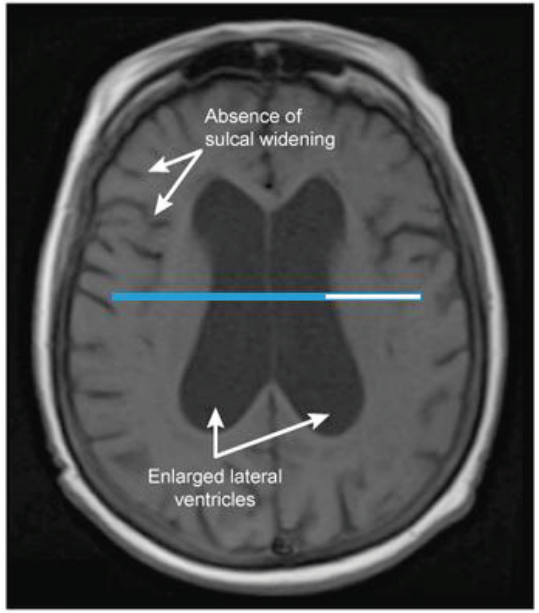
**Normal pressure hydrocephalus (NPH)**

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malformation can be delayed into early adulthood. patients typically have a long history of chronic



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**(Choice C)** A hypoplastic cerebellar vermis with cystic dilation of the fourth ventricle and a posterior fossa cyst is characteristic of congenital Dandy-Walker malformation. Although the diagnosis of Dandy-Walker malformation can be delayed into early adulthood, patients typically have a long history of chronic headaches and neurologic abnormalities (eg, unsteady gait, facial palsy).

**(Choices D and E)** Early-onset Alzheimer disease (eg, bilateral hippocampal atrophy) or frontotemporal dementia (eg, frontal/temporal lobe atrophy) can present in patients as early as the fourth decade. However, changes in memory, speech, or behavior are the predominant symptoms at presentation; movement abnormalities (eg, myoclonus, akinesia, hyperreflexia) typically develop later in the disease course.

**Educational objective:**
Huntington disease is an autosomal dominant neurodegenerative disorder that manifests with chorea (eg, involuntary, jerky, fidgety movements) and behavioral abnormalities (eg, aggressiveness, depression). Characteristic neuroimaging findings include atrophy of the caudate nuclei which results in enlargement of the frontal horns of the lateral ventricles.

| Pathology | Nervous System | Huntington disease |
|---|---|---|
| Subject | System | Topic |


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A 68-year-old woman comes to the office due to tingling and numbness affecting her hands and legs. The patient's symptoms began 2 years ago with a "pins-and-needles" sensation in the soles of her feet, which has since progressed slowly upward to the mid-calf level. Lately, she has also had similar symptoms in her fingers. The patient has a 15-year history of type 2 diabetes mellitus complicated by diabetic retinopathy. Other medical conditions include hypertension and osteoarthritis. On physical examination, ankle reflexes are absent and sensation of joint position is decreased in the toes. Romberg sign is present. A lesion involving which of the following best explains this patient's findings?

A. Axons of unmyelinated C-type fibers
B. Distal axons of large sensory fibers
C. Lumbosacral spinal nerve roots
D. Myelin of peripheral motor neurons
E. Posterior and lateral spinal tracts

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A 68-year-old woman comes to the office due to tingling and numbness affecting her hands and legs. The patient's symptoms began 2 years ago with a "pins-and-needles" sensation in the soles of her feet, which has since progressed slowly upward to the mid-calf level. Lately, she has also had similar symptoms in her fingers. The patient has a 15-year history of type 2 diabetes mellitus complicated by diabetic retinopathy. Other medical conditions include hypertension and osteoarthritis. On physical examination, ankle reflexes are absent and sensation of joint position is decreased in the toes. Romberg sign is present. A lesion involving which of the following best explains this patient's findings?

A. Axons of unmyelinated C-type fibers (6%)
B. Distal axons of large sensory fibers (49%)
C. Lumbosacral spinal nerve roots (2%)
D. Myelin of peripheral motor neurons (15%)
E. Posterior and lateral spinal tracts (25%)

Incorrect



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| Diabetic neuropathy | |
|---|---|
| **Risk factors** | • Long duration of disease<br>• Chronic hyperglycemia/poor glycemic control |
| **Pathogenesis** | • Accumulation of glycosylation end products and sorbitol → altered metabolism and increased oxidative stress<br>• Occlusion of vasa nervorum with nerve ischemia<br>• Length-dependent axonopathy |
| **Clinical manifestations** | • **Peripheral polyneuropathy**: numbness, stocking-glove paresthesia, decreased proprioception<br>• **Autonomic neuropathy**: gastroparesis, orthostasis, neurogenic bladder, erectile dysfunction<br>• **Motor neuropathy**: distal limb weakness, hammer/claw toe deformities |

This patient has numbness and paresthesias in a **stocking-glove distribution**, along with decreased proprioception (eg, decreased joint position sense) consistent with **diabetic polyneuropathy**. Diabetes


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This patient has numbness and paresthesias in a **stocking-glove distribution**, along with decreased proprioception (eg, decreased joint position sense) consistent with **diabetic polyneuropathy**. Diabetes mellitus is the most common cause of peripheral neuropathy in adults. The risk of neuropathy and other **microvascular complications** (eg, retinopathy, nephropathy) is increased in longstanding, poorly controlled diabetes; tight glycemic control can decrease the risk.

Neuronal injury occurs due to accumulation of advanced glycosylation end products, sorbitol, and other toxic substances that lead to deranged metabolism and increased oxidative stress. In addition, diabetic microangiopathy affecting the endoneurial vessels can promote nerve ischemia. This, in combination with the metabolic disturbances, leads to a **length-dependent axonopathy**, with clinical features occurring first in the longest nerves (eg, feet); symptoms vary depending on the type of nerve fibers involved:

- **Small-fiber** injury is characterized by predominance of **positive symptoms** (eg, pain, paresthesias, allodynia).
- **Large-fiber** involvement is characterized by predominance of **negative symptoms** (eg, numbness, loss of proprioception and vibration sense, sensory ataxia [eg, positive Romberg sign], diminished ankle reflexes).

Patients with diabetes can also develop autonomic neuropathy manifesting as gastrointestinal


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Patients with diabetes can also develop autonomic neuropathy, manifesting as gastrointestinal disturbances (eg, gastroparesis), orthostatic symptoms, bladder dysfunction, and erectile dysfunction. Degeneration of motor axons may also occur, leading to unbalanced strength in the extremities and hammer or claw toe deformities.

**(Choice A)** C-fibers are small, unmyelinated fibers that carry pain and temperature sensation. Diabetes can damage these fibers, leading to a reduction in pain/temperature sensation as well as burning pain. Numbness, tingling paresthesias, diminished reflexes, and sensory ataxia are more consistent with large-fiber neuropathy.

**(Choice C)** Nerve root dysfunction (ie, radiculopathy) is most commonly due to compression from disc herniation or degenerative changes in the vertebral column. The associated pain/numbness is in a dermatomal (rather than stocking-glove) distribution and is often associated with muscular weakness and atrophy.

**(Choice D)** Guillain-Barré syndrome is an immune-mediated polyneuropathy caused by demyelination of peripheral nerve fibers. It can cause paresthesias and neuropathic pain but typically presents with rapidly progressive ascending weakness. Most patients have a preceding respiratory or gastrointestinal infection (eg, *Campylobacter*).



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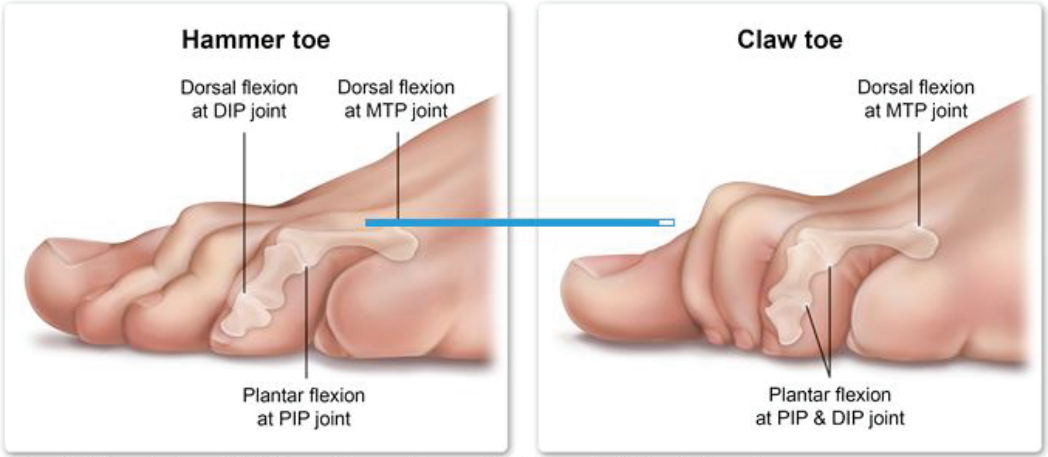
## Hammer & claw toe deformities




**DIP** = distal interphalangeal; **MTP** = metatarsophalangeal; **PIP** = proximal interphalangeal.
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**(Choice D)** Guillain-Barré syndrome is an immune-mediated polyneuropathy caused by demyelination of peripheral nerve fibers. It can cause paresthesias and neuropathic pain but typically presents with rapidly progressive ascending weakness. Most patients have a preceding respiratory or gastrointestinal infection (eg, *Campylobacter*).

**(Choice E)** Subacute combined degeneration of the spinal cord results from chronic vitamin $B_{12}$ deficiency. Manifestations in the posterior columns can include loss of proprioception, paresthesia, and sensory ataxia, but concurrent lateral corticospinal tract signs (eg, spastic paresis) and other signs of $B_{12}$ deficiency (eg, atrophic glossitis, macrocytic anemia) are typically present.

**Educational objective:**
Diabetes mellitus is the most common cause of peripheral polyneuropathy in adults. Common findings include numbness and paresthesias in a stocking-glove distribution and decreased proprioception due to degeneration of large-fiber sensory axons.

| Pathology | Nervous System | Diabetic neuropathy |
|---|---|---|
| Subject | System | Topic |

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A 46-year-old woman comes to the emergency department due to sudden-onset, severe occipital headache and nausea. The patient has a history of hypertension and cigarette smoking. Physical examination shows mild disorientation but no focal weakness, sensory loss, or cranial nerve abnormalities. Noncontrast CT scan of the head reveals diffuse hyperdensity in the subarachnoid space. CT angiography reveals a ruptured anterior communicating artery aneurysm. The patient undergoes endovascular coiling of the aneurysm. Four days later, there is sudden deterioration in her level of consciousness and new, right-sided hemiparesis is observed. Repeat CT scan shows no significant changes. Which of the following is the most likely cause of this patient's neurological deterioration?

A. Arterial thrombosis
B. Embolism
C. Hydrocephalus
D. Rebleeding
E. Vascular inflammation
F. Vasospasm



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headache and nausea. The patient has a history of hypertension and cigarette smoking. Physical examination shows mild disorientation but no focal weakness, sensory loss, or cranial nerve abnormalities. Noncontrast CT scan of the head reveals diffuse hyperdensity in the subarachnoid space. CT angiography reveals a ruptured anterior communicating artery aneurysm. The patient undergoes endovascular coiling of the aneurysm. Four days later, there is sudden deterioration in her level of consciousness and new, right-sided hemiparesis is observed. Repeat CT scan shows no significant changes. Which of the following is the most likely cause of this patient's neurological deterioration?

A. Arterial thrombosis (8%)
B. Embolism (8%)
C. Hydrocephalus (1%)
D. Rebleeding (11%)
E. Vascular inflammation (6%)
F. Vasospasm (64%)



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**Subarachnoid hemorrhage** (SAH) is a life-threatening condition that most commonly results from rupture of a saccular (berry) aneurysm. It classically manifests with the abrupt onset of severe headache **(thunderclap headache)**; confusion, loss of consciousness, and meningismus may also occur. Noncontrast head CT scan reveals blood in the subarachnoid space (between the arachnoid and pia mater).

If the patient survives the initial SAH, a number of complications (eg, rebleeding, hydrocephalus, seizures) may occur in the following days to weeks. The most common is **arterial vasospasm**, which occurs due to the release of vasoconstrictive factors from damaged erythrocytes in the subarachnoid space and the inability of damaged vascular endothelial cells to produce vasodilators (eg, nitric oxide). The resultant unopposed vasoconstriction can cause **delayed cerebral ischemia**, which manifests as a change in mental status and/or new **focal neurological deficits** 3-12 days after the SAH.

**CT scan** usually reveals **no significant changes** despite the severity of the ischemia following vasospasm. Nimodipine, a selective calcium channel blocker, is used after SAH to promote vasodilation and prevent calcium-dependent excitotoxicity, which improves outcomes by reducing the incidence and extent of ischemia due to cerebral vasospasm.


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**(Choices A, B, and E)** Although arterial thrombosis, embolism, and vascular inflammation could all cause a change in mental status and focal neurologic deficits, they are not significant complications of SAH.

**(Choice C)** Hydrocephalus may occur hours to days after SAH due to blood breakdown products obstructing the flow of cerebrospinal fluid or clogging the arachnoid villi. Patients develop signs of elevated intracranial pressure (eg, nausea/vomiting), and neuroimaging demonstrates ventricular dilation.

**(Choice D)** Rebleeding after initial SAH carries a high mortality rate and usually occurs early (<24 hours) after the initial bleed. Although symptoms can include a sudden change in level of consciousness and appearance of new neurological deficits, rebleeding is very rare 4 days after a successfully repaired aneurysmal rupture and CT scan would demonstrate newly extravasated blood.

**Educational objective:**
The most common complication of aneurysmal subarachnoid hemorrhage is vasospasm, which typically occurs 3-12 days after the initial insult and can cause delayed cerebral ischemia (eg, sudden change in mental status, new focal neurological deficits). The CT scan usually remains unchanged, unlike with rebleeding.

Pathology Nervous System Subarachnoid hemorrhage



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A Caucasian male who suffers from a severe neurological disease dies of an overwhelming respiratory infection. Autopsy shows an atrophic precentral gyrus and thin anterior roots of the spinal cord. Light microscopy reveals a severe loss of neurons in the anterior horn of the spinal cord and in the hypoglossal and ambiguous cranial nerve nuclei; corticospinal tracts stain only faintly, indicating demyelinization. The patient most likely suffered from which of the following?

- A. Amyotrophic lateral sclerosis
- B. Poliomyelitis
- C. Rabies
- D. Huntington disease
- E. Friedreich ataxia
- F. Vitamin $B_{12}$ deficiency

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A Caucasian male who suffers from a severe neurological disease dies of an overwhelming respiratory infection. Autopsy shows an atrophic precentral gyrus and thin anterior roots of the spinal cord. Light microscopy reveals a severe loss of neurons in the anterior horn of the spinal cord and in the hypoglossal and ambiguous cranial nerve nuclei; corticospinal tracts stain only faintly, indicating demyelinization. The patient most likely suffered from which of the following?

- A. Amyotrophic lateral sclerosis (69%)
- B. Poliomyelitis (17%)
- C. Rabies (2%)
- D. Huntington disease (1%)
- E. Friedreich ataxia (4%)
- F. Vitamin $B_{12}$ deficiency (3%)

Correct

69%
Answered correctly

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Time Spent

02/23/2021
Last Updated



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Amyotrophic lateral sclerosis (ALS) is the most common motor neuron disease. Combined upper motor neuron (UMN) and lower motor neuron (LMN) lesions are characteristic: damage to motor neurons of the anterior horns (LMN lesion) and demyelination of the corticospinal tracts (UMN lesion) are present. The result is denervation atrophy of the muscles (amyotrophy). The disease manifests in middle-aged people and has a progressive course. Most patients die within 5 years of diagnosis. Respiratory complications (such as aspiration pneumonia) are the most common cause of death. Important information about ALS is summarized in the table below.

| Criteria | Description |
|---|---|
| Macroscopic | Thin anterior roots<br>Mild atrophy of the precentral gyrus |
| Microscopic | Loss of neurons in the **anterior horn** (LMN lesion)<br>Degeneration and atrophy of the **lateral corticospinal tracts** (UMN lesion)<br>Loss of neurons in the motor nuclei of CN V, IX, X, XII |


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|---|---|
| Microscopic | lesion)<br>Degeneration and atrophy of the **lateral corticospinal tracts** (UMN lesion)<br>Loss of neurons in the motor nuclei of CN V, IX, X, XII<br>Muscle: denervation atrophy (small angular fibers) |
| Clinical | LMN symptoms: muscle weakness, atrophy, and fasciculation<br>UMN symptoms: spasticity, hyperreflexia, and pathologic reflexes |
| Genetic | Mutation of the gene that codes for copper-zinc superoxide dismutase (SOD1) may be implicated |
| Treatment | Riluzole<br>MOA: decreases glutamate release |


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**(Choice B)** Poliomyelitis is an enteroviral infection that damages motor neurons of the anterior horns. It is a pure lower motor neuron (LMN) disease. Clinical features include flaccid paralysis, atrophy, areflexia, and fasciculation.

**(Choice C)** The prodromal phase of rabies infection is characterized by fever, pharyngitis, and pain around the bite site. Acute encephalitis develops later. Ultimately, paralysis, confusion or hyperactivity, focal neurologic deficits, and coma occur.

**(Choice D)** Huntington disease is an autosomal dominant disorder that leads to atrophy of the caudate nucleus and putamen. It causes progressive dementia, behavioral changes, and choreiform movements.

**(Choice E)** Friedrich ataxia is an autosomal recessive disorder that manifests in children 5-15 years old. The main symptom is difficulty walking (ataxia). This disease is associated with hypertrophic cardiomyopathy, kyphoscoliosis, foot abnormalities, and diabetes mellitus.

**(Choice F)** Vitamin B 12 deficiency causes subacute combined degeneration of the dorsal (posterior) and lateral spinal columns.

**Educational objective:**

Amyotrophic lateral sclerosis (ALS) causes both upper and lower motor neuron lesions. Loss of neurons of


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**(Choice F)** Vitamin B 12 deficiency causes subacute combined degeneration of the dorsal (posterior) and lateral spinal columns.

**Educational objective:**
Amyotrophic lateral sclerosis (ALS) causes both upper and lower motor neuron lesions. Loss of neurons of the anterior horns of the spinal cord (LMN lesion) causes muscle weakness and atrophy. Demyelination of the lateral corticospinal tract (UMN lesion) leads to spasticity and hyperreflexia.

| Pathology | Nervous System | Amyotrophic lateral sclerosis |
|---|---|---|
| Subject | System | Topic |


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A 75-year-old man is brought to the emergency department due to 2 hours of left-sided chest pain and dyspnea. The patient has lived in a skilled nursing facility since developing right-sided hemiplegia, hemisensory loss, and aphasia 4 months ago. He has a history of diabetes mellitus, hypertension, and hypercholesterolemia. As an ECG is being obtained, the patient develops ventricular fibrillation and dies despite resuscitative efforts. An autopsy is performed; a coronal section of the brain is shown in the image below.

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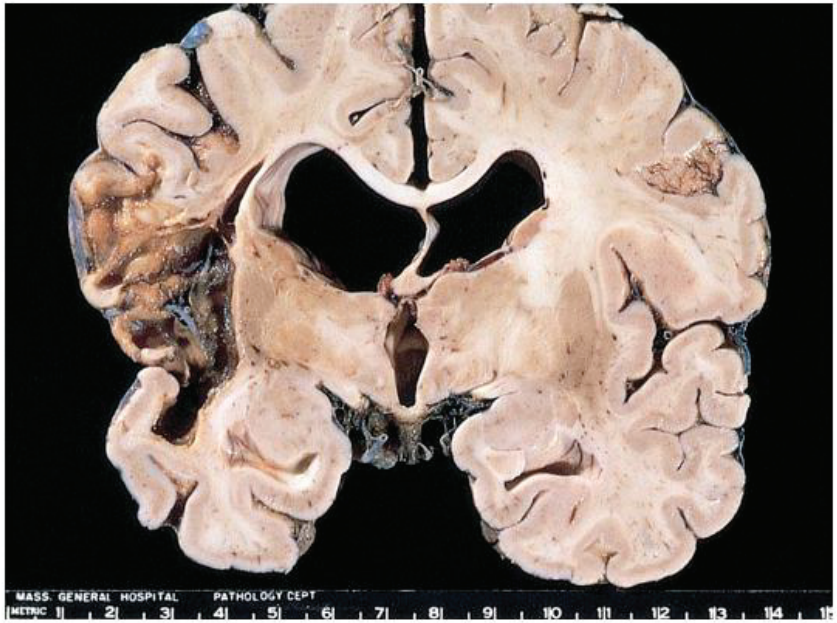


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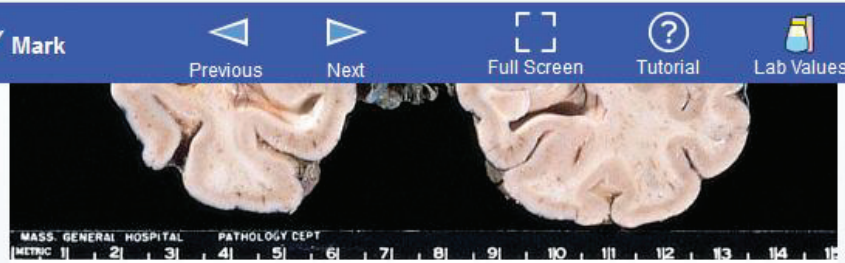


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The walls of the brain lesion are most likely composed of which of the following?

- A. Astrocytes
- B. Ependymal cells
- C. Fibroblasts
- D. Oligodendrocytes
- E. Pia mater
- F. Schwann cells

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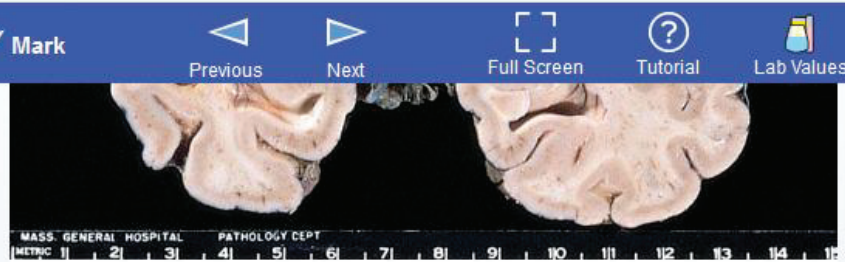


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The walls of the brain lesion are most likely composed of which of the following?

- ✓ A. Astrocytes (70%)
- B. ~~Ependymal cells~~ (3%)
- C. ~~Fibroblasts~~ (13%)
- D. ~~Oligodendrocytes~~ (8%)
- E. ~~Pia mater~~ (3%)
- F. ~~Schwann cells~~ (0%)

Correct

70%

01 min, 08 secs

02/26/2021



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| Ischemic stroke | | |
|---|---|---|
| **Time after injury** | **Microscopic changes** | **Macroscopic changes** |
| 12-24 hours | Red neurons (eosinophilic cytoplasm, pyknotic nuclei, loss of Nissl substance) | |
| 24-72 hours | Neutrophilic infiltration | |
| 3-7 days | Macrophage/microglia infiltration & phagocytosis begins | |
| 1-2 weeks | Reactive gliosis & vascular proliferation around the necrotic area | Liquefactive necrosis (1 week-1 month) |
| >2 weeks | Glial scar formation | Cystic area surrounded by dense glial fibers (>1 month) |

The coronal section of this patient's brain shows a cystic lesion caused by **ischemic stroke** involving the left cerebral hemisphere (eg, cortex, subcortical white matter, putamen). Neuropathology coronal sections


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| | | |
|---|---|---|
| | | glial fibers (> 1 month) |

The coronal section of this patient's brain shows a cystic lesion caused by **ischemic stroke** involving the left cerebral hemisphere (eg, cortex, subcortical white matter, putamen). Neuropathology coronal sections are oriented with the right side of the brain on the examiner's right side.

Thrombosis of atherosclerotic plaques involving the cerebral arteries can result in vessel occlusion with tissue hypoxia and subsequent necrosis. Ischemic neuronal injury initially causes intense cytoplasmic eosinophilia ("red neurons") followed by neutrophil infiltration a day later. After several days, macrophages/microglia are recruited to phagocytize the necrotic debris and predominate in the ensuing 2-3 weeks. Around this time, the periphery of the necrotic area becomes populated with new blood vessels and proliferating astrocytes that form a network of cytoplasmic extensions (reactive gliosis). Several **months to years** after brain infarction, the necrotic area appears as a **cystic cavity** surrounded by a wall composed of dense fibers formed by **astrocytic processes** (glial scar).

**(Choice B)** Ependymal cells are ciliated glial cells that line the ventricles and central canal of the central nervous system and make up the choroid plexus. These cells produce cerebrospinal fluid but do not directly participate in glial scar formation around old infarcts.

**(Choice C)** Large ischemic strokes may result in perivascular fibroblast infiltration with fibrotic scar


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directly participate in glial scar formation around old infarcts.

**(Choice C)** Large ischemic strokes may result in perivascular fibroblast infiltration with fibrotic scar formation within the core of the lesion. However, this region remains separated from normal brain parenchyma by a wall of reactive gliosis, which protects viable neuronal tissue from being damaged by the fibrotic inflammatory response.

**(Choice D)** Oligodendrocytes are the myelin-producing cells of the central nervous system and do not directly participate in glial scar formation around old infarcts.

**(Choice E)** The meninges (eg, pia mater) are separated from the cystic cavity created after ischemic stroke by a gliotic tissue layer (derived from the cortex) and do not participate in glial scar formation.

**(Choice F)** Schwann cells are myelin-producing cells that help guide axonal repair and regeneration in the peripheral nervous system.

**Educational objective:**
Several months to years after ischemic brain infarction, the necrotic area appears as a cystic cavity surrounded by a wall composed of dense fibers formed by astrocytic processes (glial scar).

**References**


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A 25-year-old man comes to the office due to right arm weakness. The patient injured his right shoulder several months ago in a motor vehicle accident and has had difficulty elevating his arm since. On examination, there is diminished pinprick and temperature sensation over a small area in the right upper lateral arm and prominent atrophy of the right deltoid with 3/5 strength on right shoulder abduction. Reflexes and handgrip strength are normal in the upper extremities bilaterally. This patient most likely injured which of the following nerves?

A. Axillary
B. Dorsal scapular
C. Long thoracic
D. Median
E. Musculocutaneous
F. Radial
G. Thoracodorsal
H. Ulnar



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A. Axillary
B. Dorsal scapular
C. Long thoracic
D. Median
E. Musculocutaneous
F. Radial
G. Thoracodorsal
H. Ulnar



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lateral arm and prominent atrophy of the right deltoid with 3/5 strength on right shoulder abduction. Reflexes and handgrip strength are normal in the upper extremities bilaterally. This patient most likely injured which of the following nerves?

- A. Axillary (84%)
- B. Dorsal scapular (4%)
- C. Long thoracic (1%)
- D. Median (0%)
- E. Musculocutaneous (6%)
- F. Radial (1%)
- G. Thoracodorsal (1%)
- H. Ulnar (0%)

Correct

84%

51 secs

10/11/2020



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The axillary nerve originates from the posterior cord of the brachial plexus and carries fibers from C5 and C6. It courses deep in the axilla below the shoulder joint, then runs through the quadrangular space (bounded superiorly by the teres minor, laterally by the humerus, medially by the long head of the triceps, and inferiorly by the teres major) and along the surgical neck of the posterior humerus. At this point, it gives rise to motor branches that supply the deltoid and teres minor muscles, and a sensory branch that innervates the skin over the lateral shoulder.

Axillary nerve injury most commonly occurs in the setting of shoulder trauma (eg, anterior dislocation, proximal humeral fracture). Patients often have sensory loss over the upper lateral arm and weakness on shoulder abduction due to denervation (and possibly atrophy) of the deltoid muscle.

**(Choice B)** The dorsal scapular nerve provides motor innervation to the rhomboids (retract the scapula) and levator scapulae muscles (elevate the scapula).

**(Choice C)** Long thoracic nerve injury classically occurs during axillary lymph node dissection and results in paralysis of the serratus anterior muscle, leading to winging of the scapula.

**(Choice D)** Proximal injury to the median nerve (eg, due to supracondylar humerus fracture) may result in


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in paralysis of the serratus anterior muscle, leading to winging of the scapula.

**(Choice D)** Proximal injury to the median nerve (eg, due to supracondylar humerus fracture) may result in palmar sensory loss over the first 3 digits and impairment of thumb flexion/opposition, flexion of the second/third digits, and wrist flexion/abduction.

**(Choice E)** Injury to the musculocutaneous nerve can cause sensory loss over the lateral forearm and weakened elbow flexion due to denervation of the biceps brachii and brachialis muscles.

**(Choice F)** Injury to the radial nerve at the axilla (eg, "crutch palsy") typically causes weakness of the forearm, hand, and finger extensor muscles (eg, wrist drop, absent triceps reflex) with sensory loss over the posterior arm, forearm, and dorsolateral hand.

**(Choice G)** The thoracodorsal nerve provides motor innervation to the latissimus dorsi muscle, which is responsible for shoulder extension, adduction, and internal rotation.

**(Choice H)** Ulnar nerve injury most commonly occurs at the elbow, resulting in sensory loss over the medial 1½ digits of the hand and weakness on wrist flexion/adduction, finger abduction/adduction, and flexion of the fourth/fifth digits.

**Educational objective:**


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**(Choice H)** Ulnar nerve injury most commonly occurs at the elbow, resulting in sensory loss over the medial 1½ digits of the hand and weakness on wrist flexion/adduction, finger abduction/adduction, and flexion of the fourth/fifth digits.

**Educational objective:**
Injury to the axillary nerve most commonly occurs in the setting of shoulder trauma (eg, anterior dislocation, humeral fracture) and presents with sensory loss over the lateral shoulder and weakness on shoulder abduction (due to denervation of the deltoid muscle).

**References**

- Peripheral nerve entrapment and injury in the upper extremity.
- Axillary nerve injury.



www.ncbi.nlm.nih.gov/pubmed/20082510

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A 45-year-old man is brought to the emergency department due to new-onset seizure. His family witnessed an episode of blank staring followed by a generalized tonic-clonic convulsion with tongue biting and urinary incontinence. The patient has a past medical history of seasonal asthma and takes no prescription medications. He does not use alcohol or illicit drugs. Vital signs and neurologic examination are normal. Noncontrast head CT and brain MRI are consistent with a diagnosis of cavernous hemangioma. This patient is at greatest risk of developing which of the following complications?

A. Epidural hematoma
B. Intracerebral hemorrhage
C. Ischemic stroke
D. Migraine headaches
E. Subarachnoid hemorrhage
F. Subdural hematoma

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A. Epidural hematoma (2%)
B. Intracerebral hemorrhage (54%)
C. Ischemic stroke (7%)
D. Migraine headaches (4%)
E. Subarachnoid hemorrhage (20%)
F. Subdural hematoma (9%)



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**Cavernous hemangiomas** are vascular malformations (sporadic or familial) that most commonly occur within the **brain parenchyma** above the cerebellar tentorium. They consist of clusters of dilated, thin-walled capillaries with little or no intervening nervous tissue. Patients with cavernous hemangiomas often have **seizures** and may develop progressive neurologic deficits due to mass effect with interruption of the cerebral microcirculation. These lesions also have a **tendency to bleed**, which can contribute to neurologic symptoms (eg, due to subcortical/cortical tissue irritation) and appear as an irregular hyperdense/bright mass on head CT.

**(Choice A)** Epidural hematomas usually result from rupture of the middle meningeal artery in the setting of head trauma (eg, skull fracture at the pterion).

**(Choice C)** Cavernous hemangiomas increase the risk of hemorrhagic as opposed to ischemic stroke. Ischemic stroke typically occurs in older individuals with cardiovascular risk factors (eg, diabetes mellitus, hypertension, hyperlipidemia, smoking history) due to vessel occlusion caused by thrombosis or cardioembolism.

**(Choice D)** Migraine headache is a primary headache disorder commonly seen in young women. Although migraine headaches can have a secondary cause, they have not been linked specifically to


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cardioembolism.

**(Choice D)** Migraine headache is a primary headache disorder commonly seen in young women. Although migraine headaches can have a secondary cause, they have not been linked specifically to cavernous hemangiomas.

**(Choice E)** Subarachnoid hemorrhage is usually caused by ruptured saccular aneurysms and is an infrequent consequence of bleeding vascular malformations.

**(Choice F)** Subdural hematoma results from rupture of the bridging veins in the subdural space (between the dura and arachnoid membranes) and is most commonly caused by head trauma. Vascular malformations do not typically result in subdural hematomas.

**Educational objective:**
Cavernous hemangiomas are vascular malformations that occur most commonly within the brain parenchyma; they carry an increased risk of intracerebral hemorrhage and seizure.

**References**

- CNS cavernous haemangioma: "popcorn" in the brain and spinal cord.
- Management of cerebral cavernous malformations: from diagnosis to treatment.



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A 52-year-old man is brought to the office due to social withdrawal and inability to care for himself. The patient is divorced and lives alone, and he was found to be living in disarray by his daughter, who is visiting from out of state. His neighbors and friends say the patient rarely comes out of the house or contacts them. During previous visits, his daughter noticed fidgety movements of his hands, but now he has marked jerky movements of his extremities with frequent facial grimaces. He has a history of depression with frequent angry outbursts that led to his divorce several years ago. The patient has no other medical conditions and does not use tobacco, alcohol, or illicit drugs. He was adopted and his family history is unknown. On physical examination, the patient is forgetful and has slowed mental processing. Involuntary, spasmodic movements of the hands and facial muscles are present. Deep tendon reflexes and sensation are normal. The loss of neurons supplying which of the following neurotransmitters is most specific for this patient's disease process?

A. Acetylcholine
B. Dopamine
C. GABA
D. Norepinephrine



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A. Acetylcholine
B. Dopamine
C. GABA
D. Norepinephrine
E. Serotonin

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A. Acetylcholine (13%)
B. Dopamine (24%)
C. GABA (60%)
D. Norepinephrine (0%)
E. Serotonin (0%)

Incorrect
60%
02 mins, 01 sec
09/27/2020


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This patient with behavioral abnormalities (eg, mood changes, withdrawal), cognitive impairment, and chorea (eg, jerky, fidgety, involuntary movements) most likely has **Huntington disease** (HD). HD is a neurodegenerative disorder inherited as an autosomal dominant trait and classically manifests between ages 30 and 50. Excessive **CAG trinucleotide repeats** cause a gain-of-function mutation that leads to the accumulation of abnormal huntingtin protein in neural cells.

The **inhibitory GABAergic neurons** in the caudate nuclei **(striatum)** are especially vulnerable and **atrophy** early in the course of the disease. These neurons play an important role in regulating both emotional and motor impulses from the cerebral cortex, and their loss is central to the behavioral and movement changes in HD. As HD progresses, neuronal atrophy becomes more widespread. Patients display features of advanced dementia (eg, memory loss, facial agnosia, incontinence) with bradykinesia and near-total absence of voluntary movement.

**(Choice A)** The largest concentration of acetylcholine-producing neurons in the brain is found in the amygdala (eg, nucleus basalis of Meynert). Although there are lower levels of acetylcholine in the amygdalas of patients with HD, this change is not specific to the disease (it also occurs in Alzheimer and Lewy body dementia), and atrophy of these neurons does not occur until late in the clinical course.

**(Choice B)** In HD, dopamine is typically increased, likely due to the loss of regulation by inhibitory GABA


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amygdalas of patients with HD, this change is not specific to the disease (it also occurs in Alzheimer and Lewy body dementia), and atrophy of these neurons does not occur until late in the clinical course.

**(Choice B)** In HD, dopamine is typically increased, likely due to the loss of regulation by inhibitory GABA-producing neurons. Loss of dopaminergic neurons in the substantia nigra and striatum is found in Parkinson disease.

**(Choices D and E)** Reduced concentrations of norepinephrine and serotonin in the CNS are associated with depression, which can be treated with agents (eg, SSRIs, SNRIs) that block the reuptake or degradation of these neurotransmitters.

**Educational objective:**
Huntington disease is an autosomal dominant neurodegenerative disease that leads to the accumulation of abnormal, toxic huntingtin protein in neural cells. Inhibitory GABAergic neurons in the caudate nuclei are most susceptible, and their loss is responsible for the characteristic manifestations of Huntington disease (eg, chorea, behavioral abnormalities).

| Pathology | Nervous System | Huntington disease |
|---|---|---|
| Subject | System | Topic |


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A 7-year-old boy is brought to the emergency department due to fever, headache, vomiting, and confusion. He has no prior medical conditions and is up to date with immunizations. The patient has not traveled recently, and his parents report no exposure to individuals with similar symptoms or ingestion of anything out of the ordinary. They have recently noticed several dead birds around their neighborhood. Temperature is 39 C (102.2 F). Physical examination shows neck rigidity and right lower extremity weakness with fasciculations. Cerebrospinal fluid analysis shows a leukocyte count of 200/$mm^3$ with 20% neutrophils and 80% lymphocytes. Which of the following is the most likely pathogen responsible for this patient's condition?

A. *Cryptococcus neoformans*
B. *Hemophilus influenzae*
C. Herpes simplex virus
D. Nonpolio enterovirus
E. Polio virus
F. *Streptococcus pneumoniae*



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He has no prior medical conditions and is up to date with immunizations. The patient has not traveled recently, and his parents report no exposure to individuals with similar symptoms or ingestion of anything out of the ordinary. They have recently noticed several dead birds around their neighborhood. Temperature is 39 C (102.2 F). Physical examination shows neck rigidity and right lower extremity weakness with fasciculations. Cerebrospinal fluid analysis shows a leukocyte count of 200/mm$^3$ with 20% neutrophils and 80% lymphocytes. Which of the following is the most likely pathogen responsible for this patient's condition?

A. *Cryptococcus neoformans*
B. *Hemophilus influenzae*
C. Herpes simplex virus
D. Nonpolio enterovirus
E. Polio virus
F. *Streptococcus pneumoniae*
G. West Nile virus



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Temperature is 39 C (102.2 F). Physical examination shows neck rigidity and right lower extremity weakness with fasciculations. Cerebrospinal fluid analysis shows a leukocyte count of 200/mm$^3$ with 20% neutrophils and 80% lymphocytes. Which of the following is the most likely pathogen responsible for this patient's condition?

A. ~~*Cryptococcus neoformans*~~ (27%)
B. ~~*Hemophilus influenzae*~~ (2%)
C. ~~Herpes simplex virus~~ (2%)
D. ~~Nonpolio enterovirus~~ (19%)
E. ~~Polio virus~~ (6%)
F. ~~*Streptococcus pneumoniae*~~ (1%)
G. West Nile virus (40%)

Correct

40%
55 secs
02/05/2021


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| West Nile virus | |
|---|---|
| **Clinical syndrome** | • West Nile fever: fever, headache, rash (maculopapular/morbilliform)<br>• Neuroinvasive: meningitis, encephalitis, acute asymmetric flaccid paralysis<br>  ○ Parkinsonian symptoms (eg, rigidity, bradykinesia, tremor) |
| **Transmission** | • Mosquitoes (*Culex* spp.)<br>• More common in summer/fall<br>• Warm climate (southern United States, Latin America, Africa) |
| **Risk factors** | • Older age<br>• Malignancy/organ transplant |

**West Nile virus** is an enveloped RNA virus that is found in warm climates worldwide. The virus replicates extensively within **birds** and is passed to **mosquitos** (*Culex* species) during blood feeding. Viral accumulation in mosquito salivary glands can lead to human transmission. Most infected patients develop low-level viremia that is neutralized within a week by the humoral immune response; these individuals typically remain asymptomatic. However, a minority of patients (particularly the young, elderly, or immunosuppressed) are unable to mount an effective immune response and develop significant clinical


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immunosuppressed) are unable to mount an effective immune response and develop significant clinical manifestations, including:

- **West Nile fever** – a self-limited, **flu-like illness** that is often associated with a maculopapular rash
- **Neuroinvasive disease** – the virus is neurotropic and often causes meningitis (eg, fever, headache, neck stiffness), **encephalitis** (eg, confusion, tremors, seizures), and/or **flaccid paralysis** (eg, asymmetric weakness of limbs, fasciculations). Cerebrospinal fluid usually shows a lymphocytic pleocytosis.

Most patients recover completely with supportive care, but some with neuroinvasive disease have long-term neurologic sequelae or die.

**(Choice A)** *Cryptococcus neoformans*, a fungus found in bird feces, can cause meningoencephalitis. However, most cases occur in those with severe immunosuppression (eg, advanced AIDS).

**(Choices B and F)** *Hemophilus influenzae* and *Streptococcus pneumoniae* are leading causes of acute bacterial meningitis, which is often associated with fever, headache, vomiting, and neck stiffness. However, cerebrospinal fluid usually shows a high neutrophil count. In addition, lower-motor neuron signs such as fasciculations would be atypical.


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**(Choice C)** Herpes simplex virus is a leading cause of sporadic encephalitis; it is usually characterized by confusion, focal neurologic deficits (eg, hemiparesis, dysphagia, cranial nerve defects), and seizures. It is not harbored in birds; cerebrospinal fluid usually shows elevated erythrocytes (in addition to lymphocytic pleocytosis); and lower-motor neuron signs (eg, fasciculations) are absent.

**(Choice D)** Nonpolio enteroviruses (eg, Coxsackievirus, echovirus) often cause aseptic (viral) meningitis and can occasionally cause encephalitis. However, these viruses are not associated with bird vectors and do not typically cause lower-motor neuron signs.

**(Choice E)** Polio virus is a common cause of acute, asymmetric flaccid paralysis, but it has been eliminated from the United States.

**Educational objective:**
West Nile virus is harbored in birds and transmitted to humans by mosquitos. Most patients are asymptomatic, but the virus can cause an influenza-like illness or neuroinvasive disease with meningitis, encephalitis, and flaccid paralysis.

| Microbiology | Nervous System | West Nile virus infection |
|---|---|---|
| Subject | System | Topic |



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A 34-year-old man is evaluated in the clinic due to persistent buzzing in his right ear for the past 6 months. The patient also has decreased hearing on the right side. He has had no fever, ear pain, runny nose, sore throat, or cough. The patient does not use cotton swabs and has not been exposed to loud noise. He tried using over-the-counter oral pseudoephedrine with no improvement in his symptoms. On physical examination, there is no sinus tenderness, and mucous membranes are moist without erythema or exudate. Otoscopic examination reveals normal-appearing external auditory canals bilaterally with pinkish-grey tympanic membranes. MRI of the brain reveals an intracranial tumor. This patient's lesion has most likely arisen from which of the following structures?

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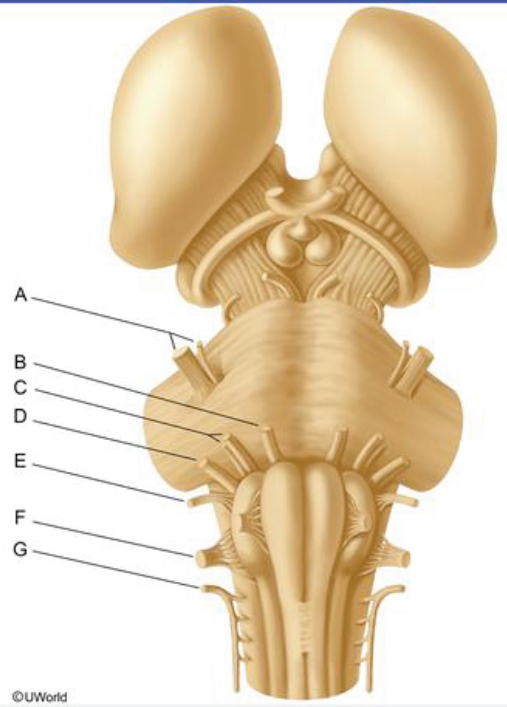


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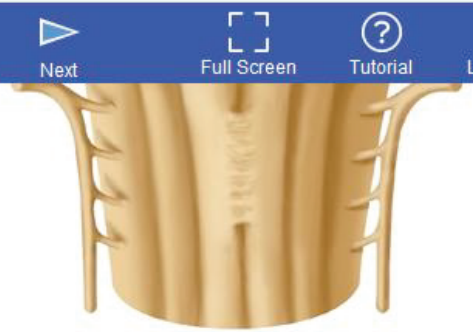

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- A. A
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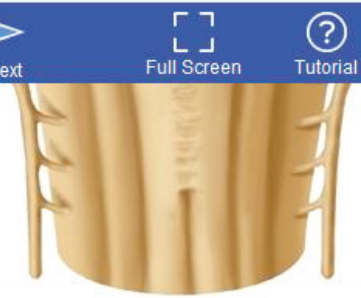

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- A. A (3%)
- B. B (2%)
- C. C (19%)
- ✓ D. D (62%)
- E. E (9%)
- F. F (2%)
- G. G (0%)

Correct

62%

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02/14/2021



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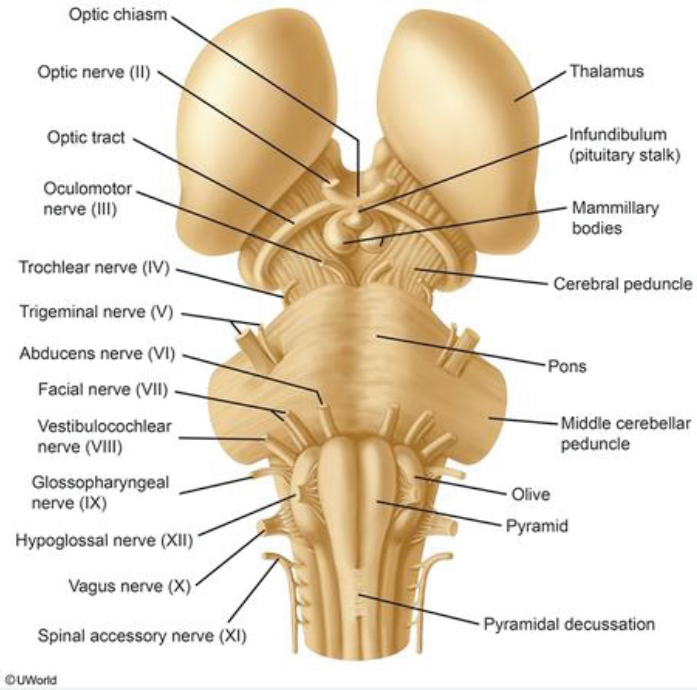


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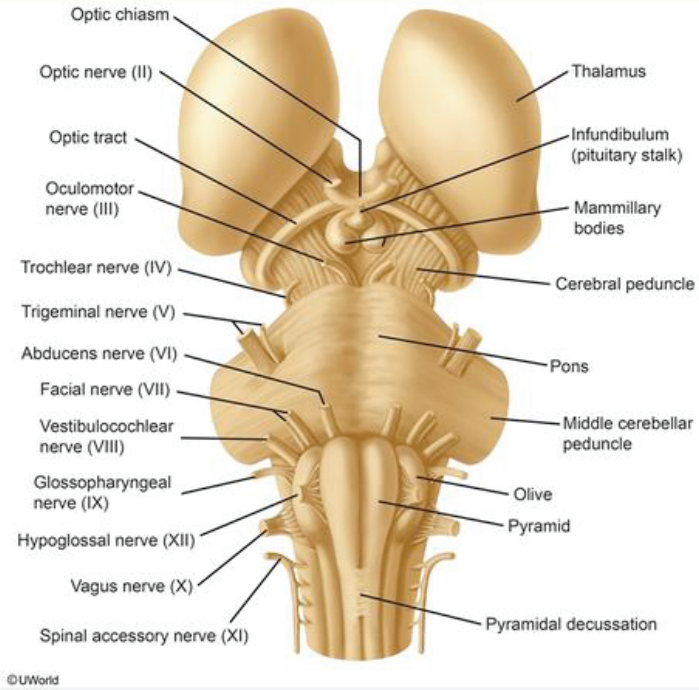


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This patient's clinical presentation is suggestive of **acoustic neuroma**, a Schwann cell-derived tumor that typically arises from the vestibular portion of the **vestibulocochlear nerve** (CN VIII). The vestibulocochlear nerve exits the brainstem from the pontomedullary junction, lateral to the facial nerve, and enters the cerebellopontine angle (between the cerebellum and lateral pons). Patients with acoustic neuroma usually have ipsilateral sensorineural **hearing loss** and **tinnitus** (ear ringing/buzzing) due to impairment of the cochlear portion of the nerve. Damage to the vestibular component may also result in vertigo, dysequilibrium, and nystagmus. Most cases present unilaterally, but bilateral acoustic neuromas are frequently seen in patients with neurofibromatosis type 2.

**(Choice A)** The trigeminal nerve (CN V) exits the brainstem from the ventrolateral pons. Injury to CN V may cause ipsilateral loss of facial sensation and the corneal reflex (afferent limb) and paralysis of the muscles of mastication.

**(Choice B)** The abducens nerve (CN VI) exits the brainstem from the pontomedullary junction medial to the facial nerve. Injury to CN VI may result in the inability to abduct the ipsilateral eye and horizontal diplopia (lack of innervation to the lateral rectus).

**(Choice C)** The facial nerve (CN VII) exits the brainstem from the ventrolateral pontomedullary junction, just lateral to the abducens nerve. Damage to CN VII may result in ipsilateral facial muscle paralysis



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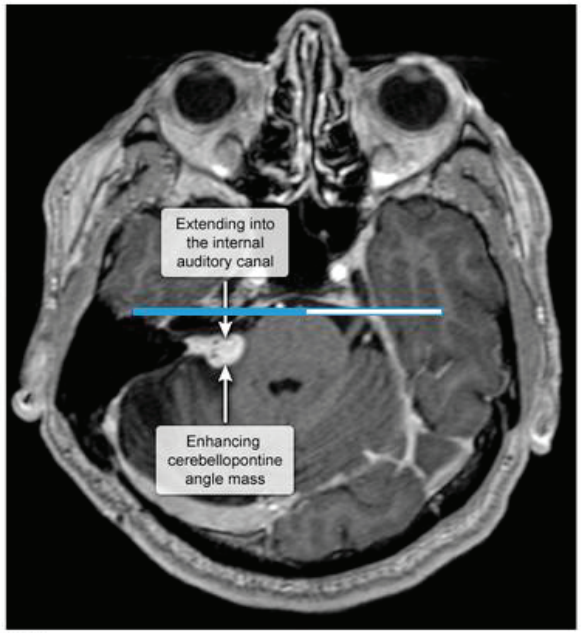
Acoustic neuroma

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**(Choice C)** The facial nerve (CN VII) exits the brainstem from the ventrolateral pontomedullary junction, just lateral to the abducens nerve. Damage to CN VII may result in ipsilateral facial muscle paralysis (upper and lower), loss of the corneal reflex (efferent limb), loss of taste in the anterior two-thirds of the tongue, and hyperacusis (lack of innervation to the stapedius).

**(Choice E)** The glossopharyngeal nerve (CN IX) exits the brainstem from the postolivary sulcus in the medulla just rostral to the vagus nerve. Injury to CN IX may result in loss of taste/sensation in the posterior one-third of the tongue and absent gag reflex (afferent limb).

**(Choice F)** The vagus nerve (CN X) exits the brainstem from the postolivary sulcus just caudal to the glossopharyngeal nerve. Damage to CN X may cause dysphonia (lack of innervation to the laryngeal muscles), impaired swallowing with inability to elevate the soft palate (lack of innervation to the pharyngeal muscles), and loss of the gag reflex (efferent limb).

**(Choice G)** Fibers of the spinal accessory nerve (CN XI) exit from the lateral medulla and upper segments of the cervical spinal cord. Injury to CN XI can cause weakness on head rotation away from the side of the lesion (lack of innervation to the sternocleidomastoid) and ipsilateral shoulder droop (lack of innervation to the trapezius).



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**(Choice C)** The facial nerve (CN VII) exits the brainstem from the ventrolateral pontomedullary junction, just lateral to the abducens nerve. Damage to CN VII may result in ipsilateral facial muscle paralysis (upper and lower), loss of the corneal reflex (efferent limb), loss of taste in the anterior two-thirds of the tongue, and hyperacusis (lack of innervation to the stapedius).

**(Choice E)** The glossopharyngeal nerve (CN IX) exits the brainstem from the postolivary sulcus in the medulla just rostral to the vagus nerve. Injury to CN IX may result in loss of taste/sensation in the posterior one-third of the tongue and absent gag reflex (afferent limb).

**(Choice F)** The vagus nerve (CN X) exits the brainstem from the postolivary sulcus just caudal to the glossopharyngeal nerve. Damage to CN X may cause dysphonia (lack of innervation to the laryngeal muscles), impaired swallowing with inability to elevate the soft palate (lack of innervation to the pharyngeal muscles), and loss of the gag reflex (efferent limb).

**(Choice G)** Fibers of the spinal accessory nerve (CN XI) exit from the lateral medulla and upper segments of the cervical spinal cord. Injury to CN XI can cause weakness on head rotation away from the side of the lesion (lack of innervation to the sternocleidomastoid) and ipsilateral shoulder droop (lack of innervation to the trapezius).



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medulla just rostral to the vagus nerve. Injury to CN IX may result in loss of taste/sensation in the posterior one-third of the tongue and absent gag reflex (afferent limb).

**(Choice F)** The vagus nerve (CN X) exits the brainstem from the postolivary sulcus just caudal to the glossopharyngeal nerve. Damage to CN X may cause dysphonia (lack of innervation to the laryngeal muscles), impaired swallowing with inability to elevate the soft palate (lack of innervation to the pharyngeal muscles), and loss of the gag reflex (efferent limb).

**(Choice G)** Fibers of the spinal accessory nerve (CN XI) exit from the lateral medulla and upper segments of the cervical spinal cord. Injury to CN XI can cause weakness on head rotation away from the side of the lesion (lack of innervation to the sternocleidomastoid) and ipsilateral shoulder droop (lack of innervation to the trapezius).

**Educational objective:**
Acoustic neuromas are Schwann cell-derived tumors that typically arise from the vestibular portion of the vestibulocochlear nerve and are commonly located at the cerebellopontine angle (between the cerebellum and lateral pons). Patients usually present with unilateral **sensorineural hearing loss** and **tinnitus.**

**References**

- Management of sporadic vestibular schwannoma.



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A 64-year-old man comes to the emergency department due to left lower extremity weakness. The patient was asymptomatic when he went to bed the night before, but he has had difficulty standing after waking up today. He has had no headache, double vision, or back pain. Medical history is significant for hypertension, diabetes mellitus, and myocardial infarction. Temperature is 37 C (98.6 F), blood pressure is 140/90 mm Hg, and pulse is 110/min and irregularly irregular. Left lower extremity examination shows motor power is 0/5, deep tendon reflexes are 3+, and Babinski sign is present. Right lower extremity examination is normal. An abnormality in which of the following structures is the most likely cause of this patient's symptoms?

A. Anterior spinal artery of the lumbosacral region
B. Left posterior inferior cerebellar artery
C. Lumbosacral spinal neuroforamina
D. Right anterior cerebral artery
E. Right middle cerebral artery


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was asymptomatic when he went to bed the night before, but he has had difficulty standing after waking up today. He has had no headache, double vision, or back pain. Medical history is significant for hypertension, diabetes mellitus, and myocardial infarction. Temperature is 37 C (98.6 F), blood pressure is 140/90 mm Hg, and pulse is 110/min and irregularly irregular. Left lower extremity examination shows motor power is 0/5, deep tendon reflexes are 3+, and Babinski sign is present. Right lower extremity examination is normal. An abnormality in which of the following structures is the most likely cause of this patient's symptoms?

A. Anterior spinal artery of the lumbosacral region (5%)
B. Left posterior inferior cerebellar artery (3%)
C. Lumbosacral spinal neuroforamina (2%)
D. Right anterior cerebral artery (74%)
E. Right middle cerebral artery (13%)

Correct

74%

01 min, 21 secs

09/19/2020



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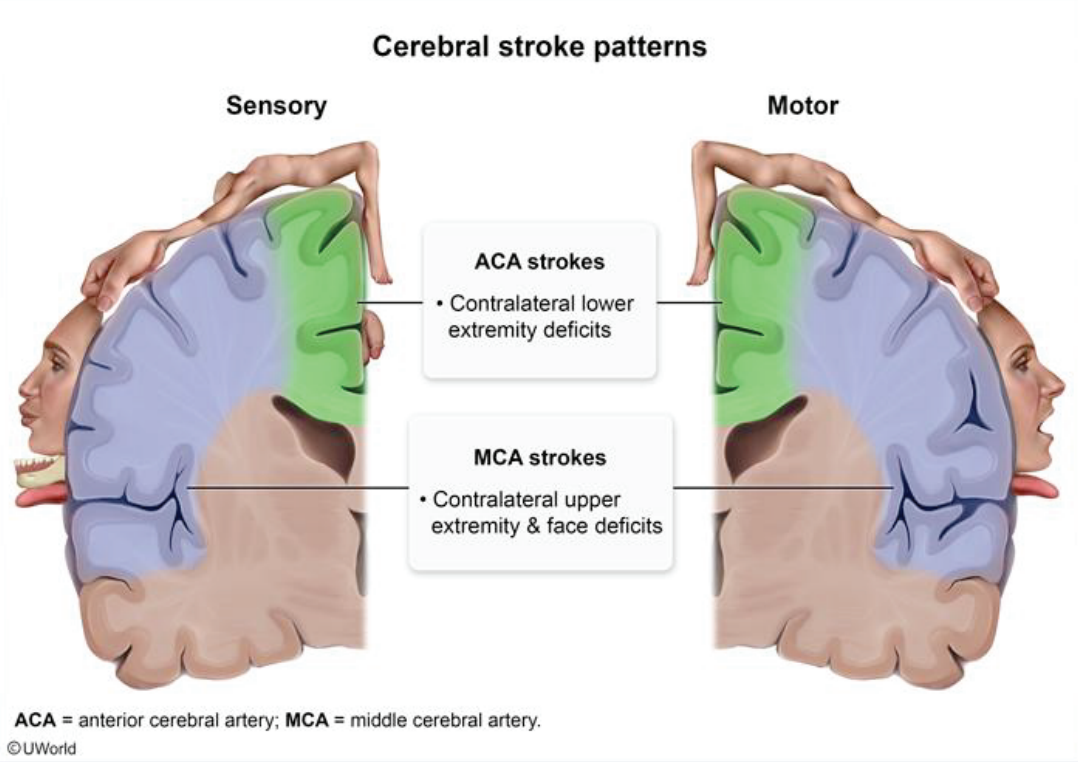


This patient with **atrial fibrillation** (irregularly irregular pulse, tachycardia) has isolated left lower extremity



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This patient with **atrial fibrillation** (irregularly irregular pulse, tachycardia) has isolated left lower extremity motor deficits, most likely caused by a **cardioembolic stroke** in the **right anterior cerebral artery** (ACA) territory. The ACA supplies the medial aspects of the frontal and parietal lobes, a region which contains the upper motor neurons responsible for contralateral lower extremity motor control. Occlusion of the ACA characteristically causes **contralateral lower limb weakness** with upper motor neuron signs (eg, hyperreflexia, Babinski sign).

The most common etiology of ACA stroke is cardiac embolization due to atrial fibrillation, which can cause blood flow stasis resulting in thrombus formation in the left atrial appendage. Atrial thromboemboli frequently travel to and obstruct branches of ACA or middle cerebral artery (MCA), causing cerebral ischemia with associated neurologic defects.

**(Choice A)** An embolic occlusion of the anterior spinal artery in the lumbosacral region would cause bilateral lower extremity weakness with hyporeflexia (ischemia of the anterior horns and corticospinal tracts) and loss of pain and temperature sensation (ischemia of the spinothalamic tracts) below the level of the lesion.

**(Choice B)** Posterior inferior cerebellar artery occlusion characteristically causes ischemia in the lateral medulla (Wallenberg syndrome) and inferior cerebellar peduncle, resulting in dysphagia, hoarseness, and vestibulocerebellar symptoms (eg, ataxia, dizziness, nystagmus)



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This patient with **atrial fibrillation** (irregularly irregular pulse, tachycardia) has isolated left lower extremity

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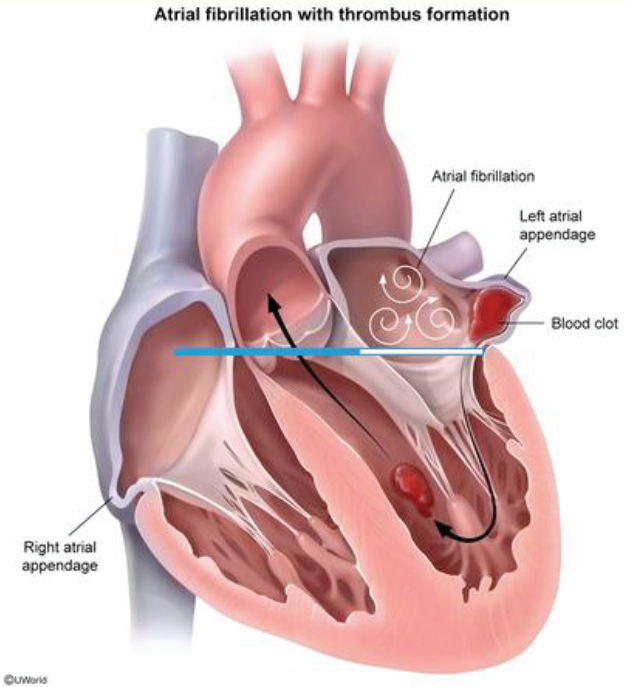


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vestibulocerebellar symptoms (eg, ataxia, dizziness, nystagmus)



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This patient with **atrial fibrillation** (irregularly irregular pulse, tachycardia) has isolated left lower extremity

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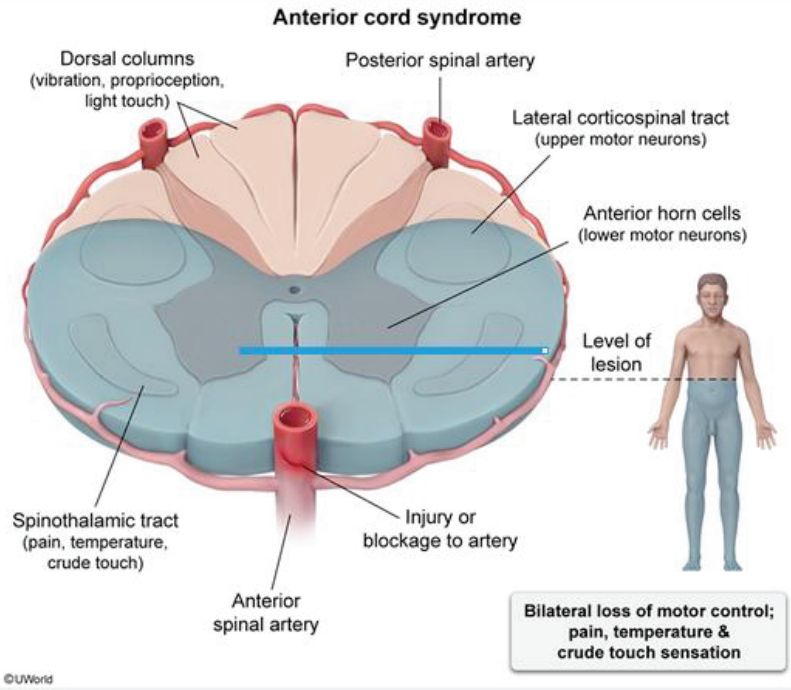


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vestibulocerebellar symptoms (eg, ataxia, dizziness, nystagmus)



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**(Choice B)** Posterior inferior cerebellar artery occlusion characteristically causes ischemia in the lateral medulla (Wallenberg syndrome) and inferior cerebellar peduncle, resulting in dysphagia, hoarseness, and vestibulocerebellar symptoms (eg, ataxia, dizziness, nystagmus).

**(Choice C)** Although lumbosacral neural foraminal stenosis can cause unilateral lower extremity weakness, compression injury of a spinal nerve root (lower motor neuron fibers) at this level would typically result in significant radicular back and leg pain with hyporeflexia.

**(Choice E)** MCA strokes predominantly affect the upper extremity and are often associated with homonymous hemianopia, aphasia, and hemineglect. Although large MCA strokes can also cause lower extremity weakness, the defects in those cases are usually extensive and involve both the upper and lower extremities (hemiparesis).

**Educational objective:**
The anterior cerebral artery (ACA) supplies the medial aspects of the frontal and parietal lobes, which contain the upper motor neurons responsible for contralateral lower extremity motor control. Thromboembolic occlusion of the ACA characteristically results in contralateral lower extremity weakness with hyperreflexia.


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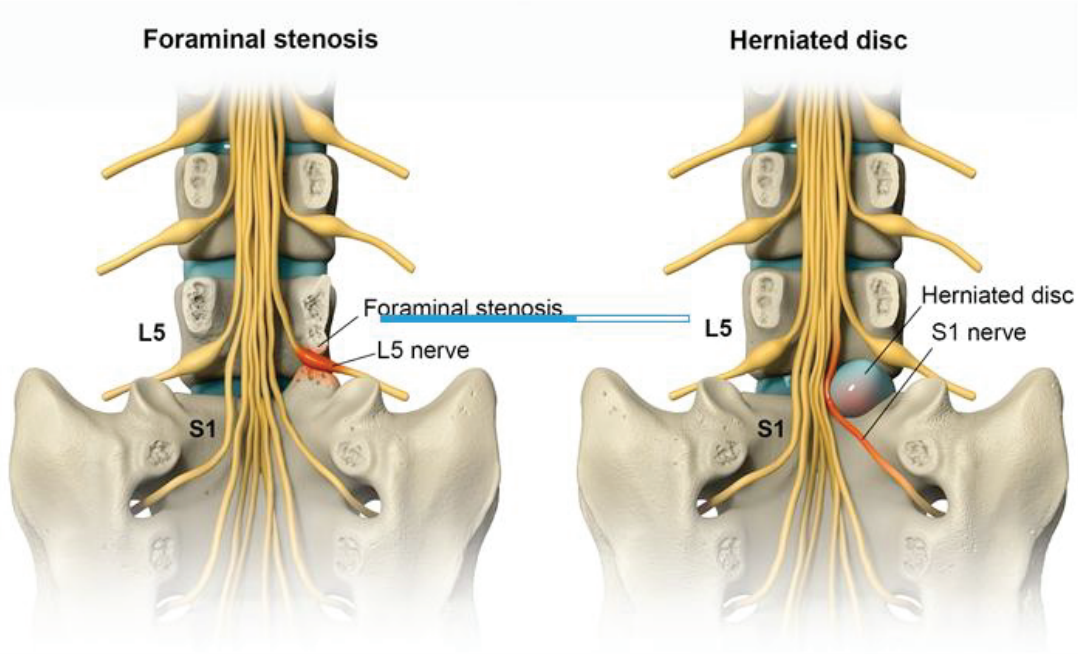
## Lumbosacral degenerative disease

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A 32-year-old man is brought to the emergency department due to weakness and tingling that started in his feet and is now at his knees. A week ago, the patient noticed that his legs felt weak while climbing stairs. Since then, the weakness has progressively worsened every day. Today, he fell twice when attempting to walk. Medical history is insignificant, except for a mild respiratory infection 2 weeks ago that resolved spontaneously. The patient does not use tobacco, alcohol, or illicit drugs. He takes no medications. Vital signs are within normal limits. Physical examination shows marked weakness in the distal muscles and moderate weakness in the proximal muscles in both legs. Deep tendon reflexes are absent at the knees. This patient's condition is most likely associated with which of the following?

A. Endomysial inflammatory infiltration
B. Endoneurial arteriole hyalinization
C. Endoneurial inflammatory infiltration
D. Mutations of a muscle structural protein gene
E. Toxin penetration through the blood-nerve barrier



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feet and is now at his knees. A week ago, the patient noticed that his legs felt weak while climbing stairs. Since then, the weakness has progressively worsened every day. Today, he fell twice when attempting to walk. Medical history is insignificant, except for a mild respiratory infection 2 weeks ago that resolved spontaneously. The patient does not use tobacco, alcohol, or illicit drugs. He takes no medications. Vital signs are within normal limits. Physical examination shows marked weakness in the distal muscles and moderate weakness in the proximal muscles in both legs. Deep tendon reflexes are absent at the knees. This patient's condition is most likely associated with which of the following?

A. Endomysial inflammatory infiltration (12%)

B. ~~Endoneurial arteriole hyalinization~~ (1%)

C. Endoneurial inflammatory infiltration (76%)

D. ~~Mutations of a muscle structural protein gene~~ (1%)

E. ~~Toxin penetration through the blood-nerve barrier~~ (8%)

Correct

76%

01 min, 23 secs

10/07/2020



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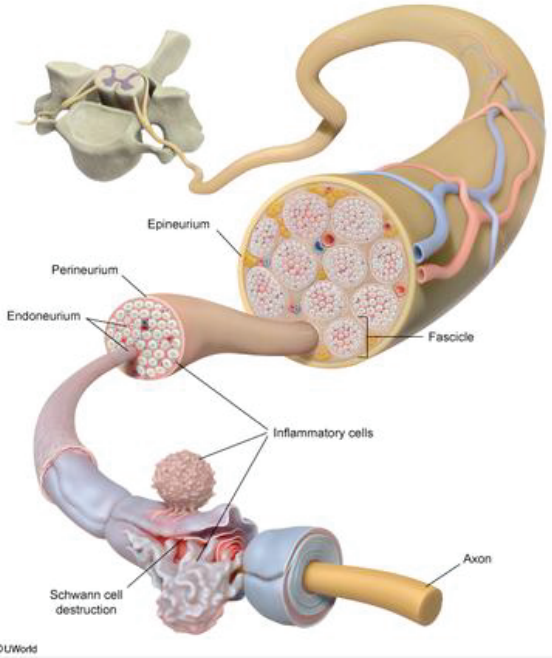
Guillain-Barré syndrome

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This patient has **ascending symmetric weakness** following a febrile illness, likely due to **Guillain-Barré syndrome** (GBS). GBS is an acute, immune-mediated, demyelinating polyneuropathy thought to be due to molecular mimicry; infectious antigens provoke an immune response that cross-reacts with the myelin of the spinal roots and peripheral nerves, resulting in demyelination of peripheral nerves. Patients develop a symmetric, ascending flaccid paralysis and areflexia leading to eventual respiratory failure; cranial nerve involvement can also occur. This is typically preceded by an upper respiratory viral illness or an episode of diarrhea (due to *Campylobacter jejuni*).

Histology demonstrates an **inflammatory infiltrate** located within the **endoneurium** (the innermost layer of connective tissue that surrounds a nerve axon and its corresponding blood vessel). The infiltrate, consisting largely of lymphocytes and macrophages, extends from the small vessels (perivenular) to the associated nerve axon. Macrophages strip the myelin sheath from the axon, and **lipid laden macrophages** are seen following the engulfment of myelin.

**(Choice A)** Endomysial inflammatory infiltration is characteristic of polymyositis (an immune-mediated inflammatory myopathy). Patients develop symmetric weakness; however, weakness is greater proximally than distally.

**(Choice B)** Hyalinization of the nerve arterioles leads to ischemic nerve injury and is a cause of diabetic



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**(Choice B)** Hyalinization of the nerve arterioles leads to ischemic nerve injury and is a cause of diabetic neuropathy. However, this occurs over an extended time (decades) in patients with long-standing, uncontrolled diabetes.

**(Choice D)** Mutations in the gene that codes for the muscle protein dystrophin can cause either a complete absence of this protein (Duchenne muscular dystrophy) or its decreased synthesis (Becker muscular dystrophy). Both of these diseases cause progressive weakness and lead to eventual respiratory failure but weakness is worse proximally and patients present in early childhood with a waddling gait and calf enlargement.

**(Choice E)** *Corynebacterium diphtheriae* can cause neuropathies due to Diphtheria toxin penetration through the blood-nerve barrier; however, diphtheria usually presents as pharyngitis with pseudomembrane formation and stridor. In addition, the neuropathy typically affects the cranial nerves prior to the peripheral nerves.

**Educational objective:**
Guillain-Barré syndrome is an acute demyelinating polyneuropathy. It is thought to be due to molecular mimicry and is commonly preceded by an upper respiratory viral illness or gastroenteritis. Segmental demyelination of the peripheral nerves and an endoneural inflammatory infiltrate are seen on light


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uncontrolled diabetes.

**(Choice D)** Mutations in the gene that codes for the muscle protein dystrophin can cause either a complete absence of this protein (Duchenne muscular dystrophy) or its decreased synthesis (Becker muscular dystrophy). Both of these diseases cause progressive weakness and lead to eventual respiratory failure but weakness is worse proximally and patients present in early childhood with a waddling gait and calf enlargement.

**(Choice E)** *Corynebacterium diphtheriae* can cause neuropathies due to Diphtheria toxin penetration through the blood-nerve barrier; however, diphtheria usually presents as pharyngitis with pseudomembrane formation and stridor. In addition, the neuropathy typically affects the cranial nerves prior to the peripheral nerves.

**Educational objective:**
Guillain-Barré syndrome is an acute demyelinating polyneuropathy. It is thought to be due to molecular mimicry and is commonly preceded by an upper respiratory viral illness or gastroenteritis. Segmental demyelination of the peripheral nerves and an endoneural inflammatory infiltrate are seen on light microscopy.


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A 45-year-old man comes to the physician because of involuntary movements and behavioral disturbance. He has frequent, jerky, irregular movements of his upper extremities that have progressively worsened over the past month. His family and friends also say that he has become increasingly irritable over the past year. Genetic testing shows a mutation affecting the huntingtin protein that causes transcriptional repression of a number of other genes. Which of the following mechanisms is most likely responsible for the decreased gene expression seen in this patient?

A. DNA hypomethylation
B. Histone deacetylation
C. Loss of normal huntingtin protein function
D. Mutation of homeodomain genes
E. Thymidine dimerization

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A 45-year-old man comes to the physician because of involuntary movements and behavioral disturbance. He has frequent, jerky, irregular movements of his upper extremities that have progressively worsened over the past month. His family and friends also say that he has become increasingly irritable over the past year. Genetic testing shows a mutation affecting the huntingtin protein that causes transcriptional repression of a number of other genes. Which of the following mechanisms is most likely responsible for the decreased gene expression seen in this patient?

A. ~~DNA hypomethylation~~ (12%)
B. Histone deacetylation (42%)
C. Loss of normal huntingtin protein function (34%)
D. Mutation of homeodomain genes (7%)
E. Thymidine dimerization (2%)

Correct

42%
Answered correctly

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Last Updated



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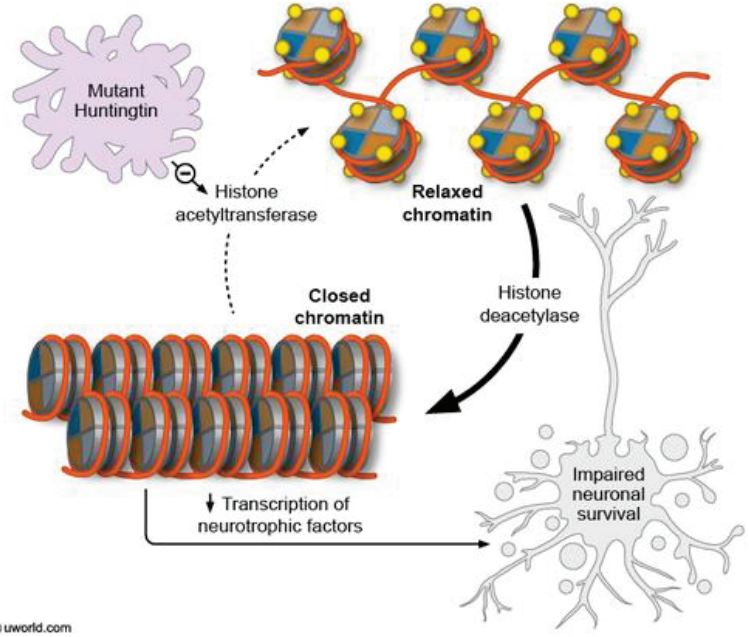
Transcriptional repression in Huntington disease

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neurotrophic factors



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**Huntington disease** is an autosomal-dominant neurodegenerative disease caused by an increase in the number of **CAG trinucleotide repeats** in the gene that codes for the **huntingtin** protein. Expansion of the protein's polyglutamine region results in a **gain-of-function** that leads to pathological interaction with other proteins, including various transcription factors.

**Transcriptional repression (silencing)** is one of the mechanisms by which mutated huntingtin is thought to cause disease. Regulation of transcription occurs in part due to the presence of histones, small proteins that complex with DNA to help compact the strands. Histones can undergo a variety of modifications (eg, methylation, acetylation, phosphorylation) that affect the accessibility of the genome for transcription. Acetylation of histones weakens the DNA-histone bond and makes DNA segments more accessible for transcription factors and RNA polymerases, enhancing gene transcription. In Huntington disease, abnormal huntingtin causes increased **histone deacetylation**, silencing the genes necessary for neuronal survival. As a result, one of the treatment options under investigation includes histone deacetylase inhibitors that help upregulate survival genes.

**(Choice A)** DNA methylation is an epigenetic modification that acts to inhibit gene transcription. Hypermethylation of the promotor region of a gene results in transcriptional silencing; hypomethylation improves gene expression.

**(Choice C)** The manifestations of Huntington disease are caused by a deleterious gain-of-function


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**(Choice C)** The manifestations of Huntington disease are caused by a deleterious gain of function mutation. Although the normal function of huntingtin is not completely understood, it is known to play a critical role in embryonic development; loss of huntingtin results in embryonic death.

**(Choice D)** Homeodomain (homeobox) genes are critical for the sequential development of organs and tissues along the body axis during embryogenesis. Mutations affecting these genes cause alterations in body structure, leading to congenital malformations or spontaneous abortion.

**(Choice E)** Thymidine dimerization is a mechanism of DNA damage induced by ultraviolet radiation.

**Educational objective:**

Hypo-acetylated histones bind tightly to DNA and prevent transcription of genes in their associated regions. Alteration of gene expression in Huntington disease occurs in part due to deacetylation of histones. This prevents the transcription of certain genes that code for neurotrophic factors, contributing to neuronal cell death.

**References**

- Mechanisms of disease: histone modifications in Huntington's disease.
- Epigenetic mechanisms of neurodegeneration in Huntington's disease.


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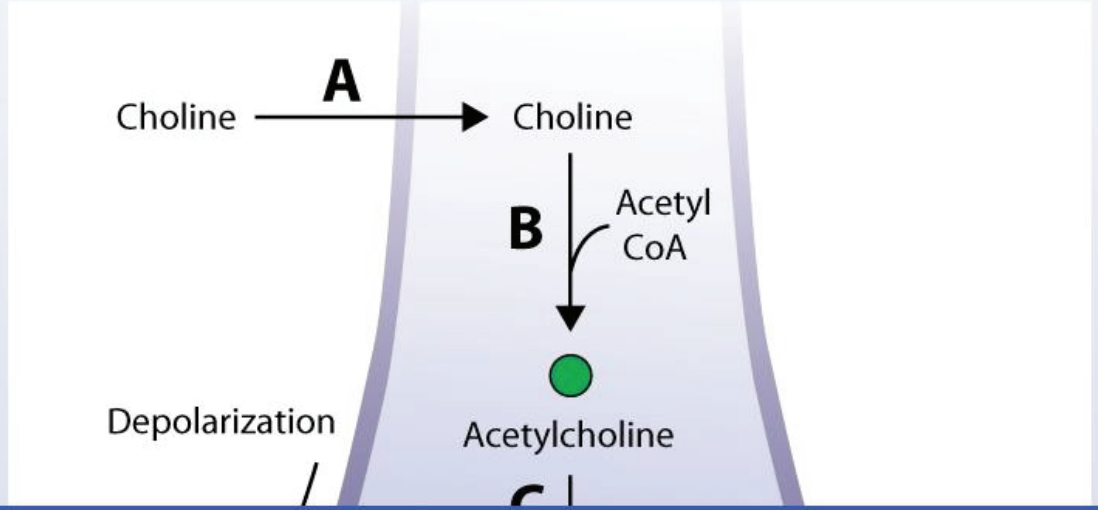
A 55-year-old farmer is brought to the emergency department after his daughter found him confused and disoriented in the tool shed at home. He has been otherwise healthy and does not take any medications. On physical examination, blood pressure is 110/70 mm Hg and pulse is 50/min. The patient's pupils are symmetric, 2 mm, and reactive to light. His eyes are tearing considerably. There are scattered wheezes bilaterally on lung auscultation. The patient's skin is clammy and he is sweating profusely. Impairment of which of the following steps at the neuromuscular junction is most likely responsible for his presentation?





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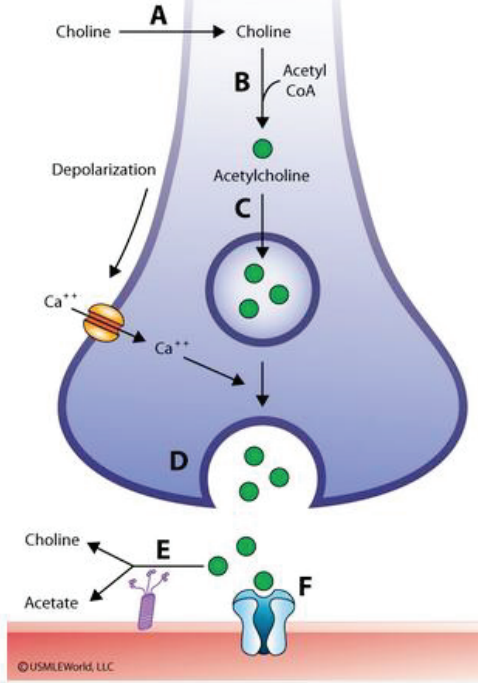


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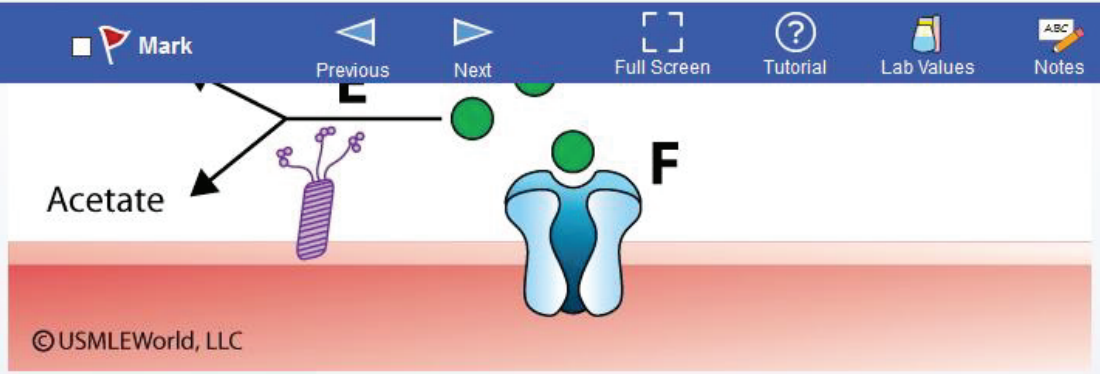


- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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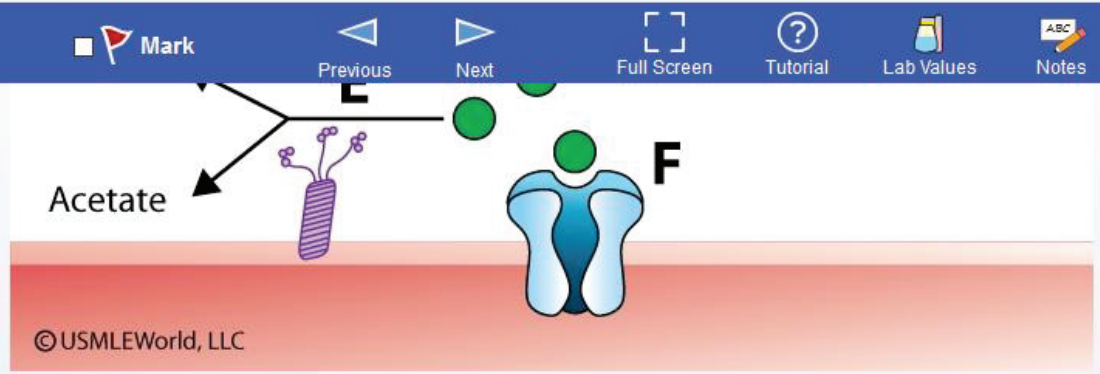


- A. A (0%)
- B. B (1%)
- C. C (1%)
- D. D (5%)
- ✓ E. E (84%)
- F. F (6%)

Correct

84%

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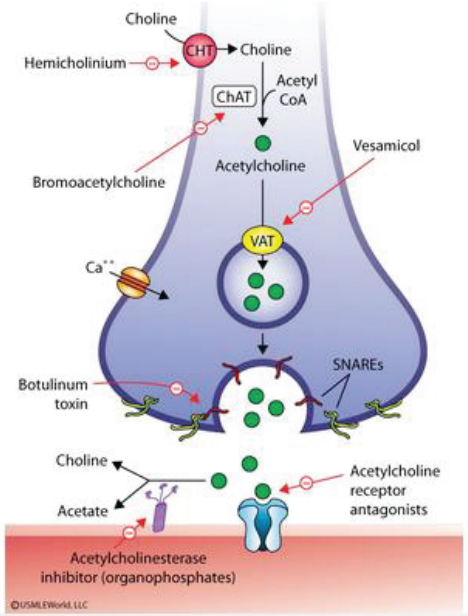
Inhibitors of acetylcholine neurotransmission

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This patient's confusion, miosis and lacrimation, bradycardia, diaphoresis, and bronchospasm (bilateral wheezes) indicate a state of global muscarinic **cholinergic overstimulation**. This can be the result of a pharmacologic cholinomimetic (eg, carbachol, methacholine) or **cholinesterase inhibitor** (blocks breakdown of endogenous acetylcholine).

**Organophosphates** are cholinesterase inhibitors that are widely used as pesticides in agriculture. They are lipid soluble; rapidly absorbed via oral, cutaneous, and inhalational routes of exposure; and readily penetrate the blood brain barrier. Organophosphates are **irreversible** cholinesterase inhibitors; they elicit cholinergic stimulation that lasts until new cholinesterase enzymes are synthesized. Organophosphate poisoning is treated with muscarinic antagonists (eg, **atropine**) and **pralidoxime** (PAM), a drug that reactivates acetylcholinesterase by binding organophosphates and decoupling them from the enzyme.

**(Choices A, B, and C)** Blockade of neuronal choline uptake and inhibition of choline acetyltransferase would diminish acetylcholine synthesis. Blockade of acetylcholine uptake into axoplasmic vesicles would reduce acetylcholine release from presynaptic neurons. A decrease in acetylcholine synthesis or release would have effects opposite those observed in this patient.

**(Choice D)** Botulinum toxin inhibits acetylcholine release from presynaptic neurons. Botulinum toxicity



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**(Choices A, B, and C)** Blockade of neuronal choline uptake and inhibition of choline acetyltransferase would diminish acetylcholine synthesis. Blockade of acetylcholine uptake into axoplasmic vesicles would reduce acetylcholine release from presynaptic neurons. A decrease in acetylcholine synthesis or release would have effects opposite those observed in this patient.

**(Choice D)** Botulinum toxin inhibits acetylcholine release from presynaptic neurons. Botulinum toxicity (botulism) causes descending skeletal muscle paralysis, typically beginning with the cranial nerves.

**(Choice F)** Atropine is an anticholinergic agent used pharmacologically to block post-junctional acetylcholine receptors and is the antidote for organophosphate poisoning.

**Educational objective:**
Organophosphates are cholinesterase inhibitors that are widely used as pesticides in agriculture. They inhibit the breakdown of acetylcholine, leading to a state of cholinergic excess. Symptoms of organophosphate poisoning include salivation, lacrimation, diaphoresis, bradycardia, and bronchospasm.

**References**

- Organophosphate and carbamate poisoning.

| Biochemistry | Nervous System | Organophosphate poisoning |
|---|---|---|
| Subject | System | Topic |



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Experimental animals are immunized to protein fragments derived from peripheral nerve myelin. Subsequent analysis finds evidence of a T-cell response as well as production of autoantibodies against nonprotein antigens. This leads to segmental demyelination of peripheral nerves in the animals. The experimentally induced condition is most analogous to which of the following?

A. Duchenne muscular dystrophy
B. Guillain-Barré syndrome
C. Lambert-Eaton syndrome
D. Neuropathic beriberi
E. Subacute combined degeneration
F. Werdnig-Hoffman syndrome

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Experimental animals are immunized to protein fragments derived from peripheral nerve myelin. Subsequent analysis finds evidence of a T-cell response as well as production of autoantibodies against nonprotein antigens. This leads to segmental demyelination of peripheral nerves in the animals. The experimentally induced condition is most analogous to which of the following?

A. Duchenne muscular dystrophy (0%)
✓ B. Guillain-Barré syndrome (92%)
C. Lambert-Eaton syndrome (2%)
D. Neuropathic beriberi (0%)
E. Subacute combined degeneration (2%)
F. Werdnig-Hoffman syndrome (1%)

Correct

92% Answered correctly

41 secs Time Spent

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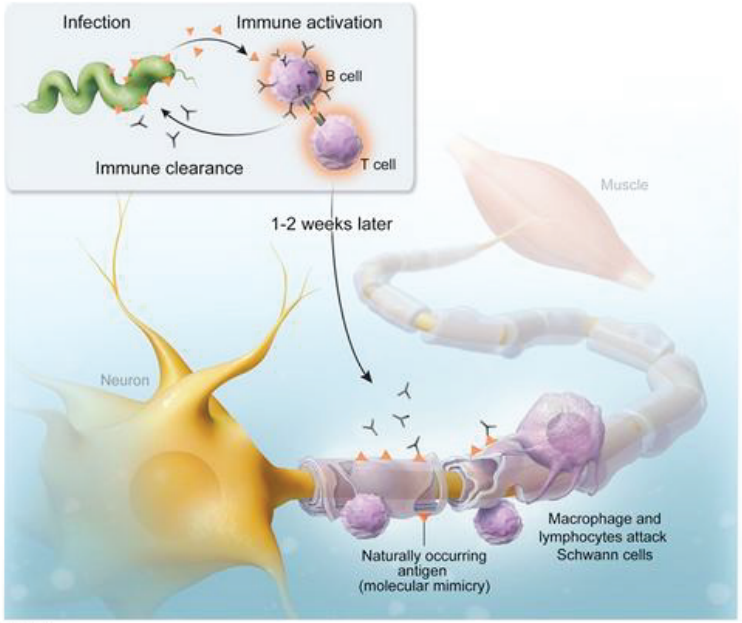
Exhibit Display

Pathogenesis of Guillain-Barré Syndrome

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Demyelination of peripheral nerves in response to immune challenge with a myelin-like substance is a pathogenic mechanism similar to **Guillain-Barré syndrome** (GBS). GBS is thought to be due to **molecular mimicry**, in which an infectious agent contains a ganglioside-like substance in its lipopolysaccharide layer. Antibodies formed against this substance and activated T-cells cross-react with the ganglioside components of myelin and Schwann cells. **Segmental demyelination** and an **endoneurial inflammatory infiltrate** composed of lymphocytes and macrophages are seen on light microscopy.

GBS manifests as **ascending, symmetric muscle weakness** that often occurs after a gastrointestinal (eg, *Campylobacter jejuni*) or upper respiratory infection. Deep tendon reflexes are decreased or absent (areflexia), and the paralysis may ascend to the cranial nerves (particularly cranial nerve VII). Paralysis of respiratory muscles is fatal without supportive care.

**(Choice A)** Duchenne muscular dystrophy is an X-linked muscular dystrophy that affects boys and is caused by a frameshift mutation of the dystrophin gene. Clinical features include progressive weakness and a waddling gait with onset in childhood. Muscle biopsy shows degeneration of muscle fibers and replacement with fat and connective tissue; peripheral nerves are not involved.



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replacement with fat and connective tissue; peripheral nerves are not involved.

**(Choice C)** Lambert-Eaton syndrome, often seen as a paraneoplastic syndrome in patients with small cell carcinoma of the lung, presents with weakness that improves with muscular repetition. It is caused by autoantibodies that react with the voltage-gated calcium channels on the presynaptic membrane, hampering the release of acetylcholine. The axons are not affected.

**(Choice D)** Beriberi (thiamine deficiency) is characterized by weakness, areflexia, pain, and paresthesias that are worse in the distal lower limbs. Beriberi can cause demyelination of peripheral nerves; however, unlike Guillain-Barré syndrome, no endoneurial inflammation is present.

**(Choice E)** Subacute combined degeneration occurs due to vitamin $B_{12}$ deficiency and leads to degeneration of dorsal columns and lateral cerebrospinal tracts. Patients develop distal, progressive weakness and ataxia but the symptoms are slowly progressive (unlike GBS, which progresses rapidly). In addition, subacute combined degeneration is associated with spasticity, paresthesia, and a macrocytic anemia.

**(Choice F)** Werdnig-Hoffman syndrome (spinal muscle atrophy type 1) is due to degeneration of the anterior horn cells that is caused by a mutation in the *SMN1* gene. Werdnig-Hoffman syndrome causes symmetric progressive weakness, but the weakness is more prominent proximal>distal and typically occurs


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weakness and ataxia but the symptoms are slowly progressive (unlike GBS, which progresses rapidly). In addition, subacute combined degeneration is associated with spasticity, paresthesia, and a macrocytic anemia.

**(Choice F)** Werdnig-Hoffman syndrome (spinal muscle atrophy type 1) is due to degeneration of the anterior horn cells that is caused by a mutation in the *SMN1* gene. Werdnig-Hoffman syndrome causes symmetric progressive weakness, but the weakness is more prominent proximal>distal and typically occurs in childhood.

**Educational objective:**
Guillain-Barré syndrome is an acute, demyelinating polyneuropathy thought to be caused by molecular mimicry. Antibodies formed against infectious agents cross-react with myelin and Schwann cells, leading to immune-mediated demyelination. Light microscopy shows segmental demyelination and an endoneurial inflammatory infiltrate composed of lymphocytes and macrophages.

| Pathology | Nervous System | Guillain Barre syndrome |
|---|---|---|
| Subject | System | Topic |

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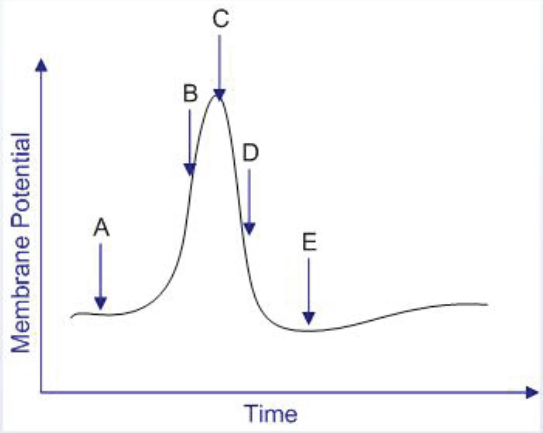
Neurophysiologists are studying recordings of the membrane potential from a giant squid axon. A portion of their recordings is shown on the slide below.




The membrane is most permeable to potassium ions at which of the following points?

A. A
B. B
C. C



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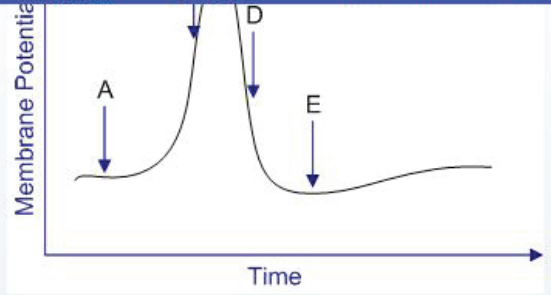


The membrane is most permeable to potassium ions at which of the following points?

- A.A
- B.B
- C.C
- D.D
- E.E

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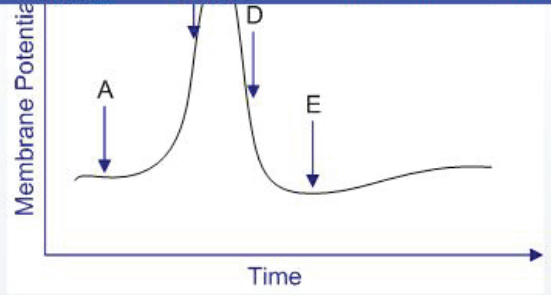


The membrane is most permeable to potassium ions at which of the following points?

- A.A (2%)
- B.B (2%)
- C.C (17%)
- ✓ D.D (67%)
- E.E (8%)

Correct

67%

59 secs

12/26/2020



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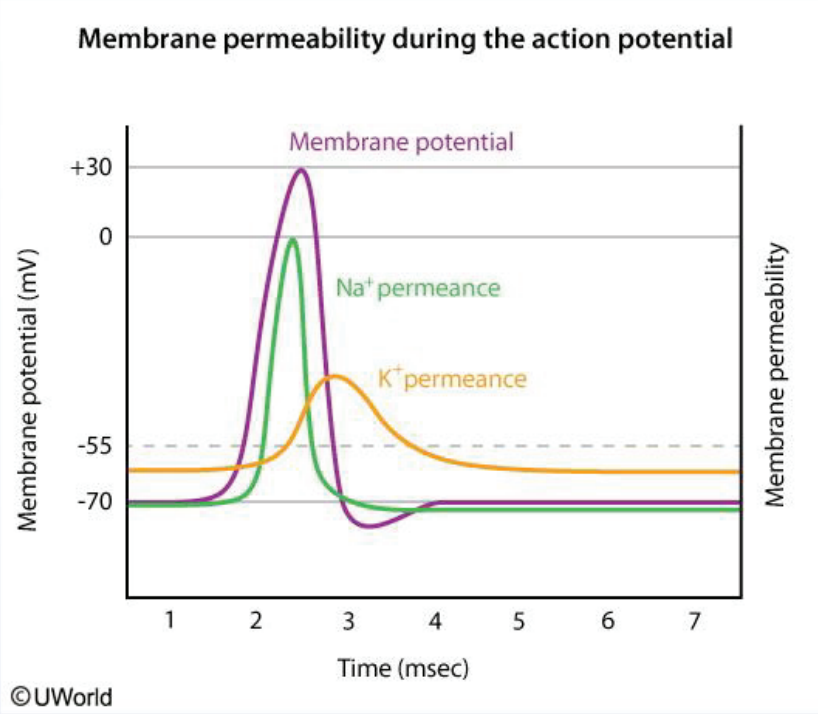


The graph depicts the potential voltage changes across a cell membrane; these changes (depolarization, repolarization, hyperpolarization, and resting potential) are collectively known as the action potential. The


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The graph depicts the potential voltage changes across a cell membrane; these changes (depolarization, repolarization, hyperpolarization, and resting potential) are collectively known as the action potential. The action potential occurs due to changes in the membrane permeability to $Na^+$ and $K^+$ ions. The membrane potential of an excitable cell (eg, nerve and muscle) cycles through the following stages:

1. **Resting potential (Choice A):** Usually equal to -70 mV. It is maintained by high resting membrane permeability to $K^+$ and low permeability to $Na^+$. $K^+$ efflux occurs via non-gated $K^+$ channels (leak channels). While at the resting potential, the inner side of the membrane is negatively charged with respect to the outer surface of the membrane.
2. **Depolarization:** Occurs due to opening of voltage-gated $Na^+$ channels with rapid influx of $Na^+$ into the cell. The large influx of $Na^+$ leads to an increased positive charge inside the membrane known as depolarization **(Choice B)**. Overshoot refers to the maximal value of the action potential during which the membrane potential obtains a positive value (approximately +35 mV) **(Choice C)**.
3. **Repolarization (Choice D):** Results from closure of $Na^+$ channels and simultaneous opening of $K^+$ channels. This causes a sharp decrease in the membrane permeability to $Na^+$ and a significant increase in $K^+$ permeance that exceeds that of the resting membrane. $K^+$ efflux is responsible for returning the membrane potential back to the resting potential



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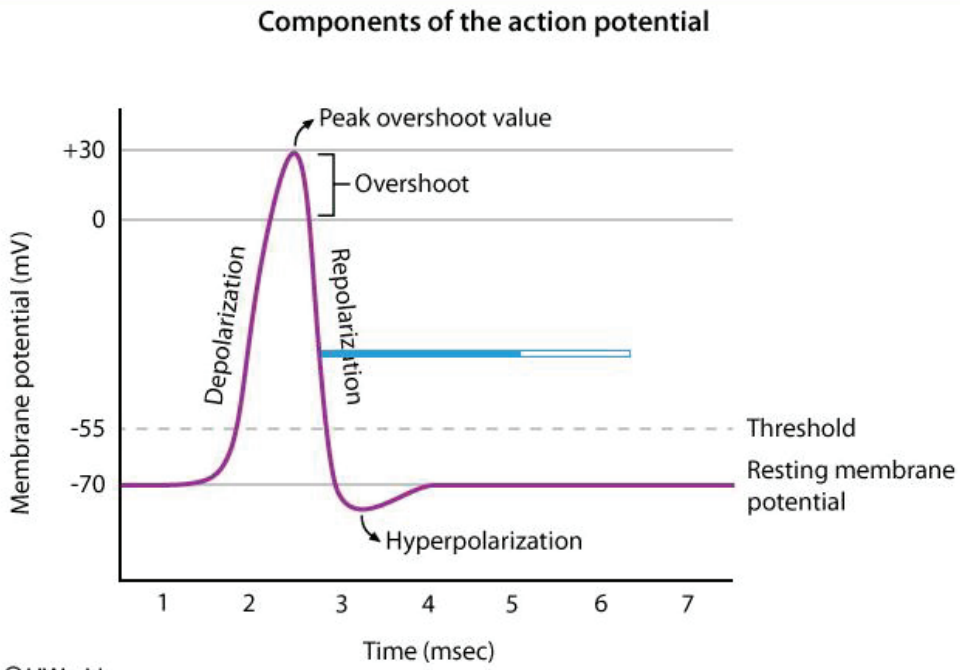


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returning the membrane potential back to the resting potential



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channels. This causes a sharp decrease in the membrane permeability to $Na^+$ and a significant increase in $K^+$ permeance that exceeds that of the resting membrane. $K^+$ efflux is responsible for returning the membrane potential back to the resting potential.

4. **Hyperpolarization (Choice E):** Occurs because the voltage-gated $K^+$ channels remain open for a short time after repolarization is completed. The membrane potential thus becomes more negative than the normal resting potential and approaches the $K^+$ equilibrium potential of -85 mV. When the voltage-gated $K^+$ channels close, the membrane potential returns to the resting value maintained by the non-gated $K^+$ channels.

**Educational objective:**

The action potential results from changes in the membrane permeability to $K^+$ and $Na^+$ ions. Depolarization results from massive influx of $Na^+$ through voltage-gated $Na^+$ channels. Repolarization occurs due to closure of voltage-gated $Na^+$ channels and opening of voltage-gated $K^+$ channels. $K^+$ ion permeance is highest during the repolarization phase of the action potential.

| Physiology | Nervous System | Resting membrane potential and action potential |
|---|---|---|
| Subject | System | Topic |


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A 12-year-old girl is brought to the office by her mother due to unusual nighttime behavior. The mother reports that once or twice a month over the past year she has found her daughter walking around the house between the hours of midnight and 2 AM. The mother says, "Although her eyes are open, she appears to be in a daze and doesn't respond to me. I guide her back to bed and she goes back to sleep, but I worry that she could get hurt or fall down the stairs if I'm not there." The girl has no recollection of the events. Which of the following EEG patterns is characteristic of the sleep stage associated with this behavior?

A. Alpha waves
B. Beta waves
C. Delta waves
D. K complexes
E. Sleep spindles

Submit



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A. ~~Alpha waves~~ (4%)
B. Beta waves (8%)
✓ C. Delta waves (74%)
D. ~~K complexes~~ (7%)
E. ~~Sleep spindles~~ (6%)

Correct

74%
Answered correctly

50 secs
Time Spent

02/15/2021
Last Updated



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| Sleep stages | | |
|---|---|---|
| | **EEG pattern & frequencies** | **Characteristics/pathology** |
| **Non-REM stage 1 (N1)** | • Theta waves (4-7.9 Hz) | • Wakefulness-sleep transition<br>• Easy to wake |
| **Non-REM stage 2 (N2)** | • Theta waves (4-7.9 Hz)<br>• Sleep spindles & K-complexes | • Largest percentage of sleep |
| **Non-REM stage 3 (N3)** | • Delta waves (<4 Hz) | • Prominent 1st half of night<br>• Difficult to wake<br>• Sleepwalking & night terrors |
| **REM** | • EEG resembles wakefulness<br>• Occasional sawtooth waves | • Prominent 2nd half of night<br>• Dreams, REMs, muscle atonia<br>• REM sleep behavior disorder & nightmare disorder |


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This girl's nighttime ambulation associated with incomplete arousal and amnesia for the event is consistent with **sleepwalking**, a non-REM (NREM) parasomnia. Sleepwalking is more common in children, peaks at age 8-12, and often remits spontaneously. **NREM-related parasomnias** such as sleepwalking and sleep terrors occur during **deep, slow-wave sleep**. Deep, slow-wave sleep is more prominent during the first half of the night and, as a result, NREM-related parasomnias occur more commonly during this time.

Sleep is divided into NREM and REM sleep. Most dreams occur during REM sleep. NREM sleep is further divided into 3 substages based on depth of sleep (N1, N2, and N3). Brain waves of different frequencies are associated with different stages of sleep. **Delta waves** (frequency up to 3.99 Hz) are characteristic of deep, slow-wave sleep (stage N3). Alpha and beta waves are characteristic of wakefulness and REM sleep **(Choices A and B)**. K complexes and Sleep spindles are characteristic of stage N2 (light, stable sleep) **(Choices D and E)**.

**Educational objective:**
Sleepwalking, a common non-REM parasomnia of childhood, occurs during slow-wave sleep (stage N3), which is characterized by delta waves on EEG. Sleepwalking typically occurs during the first half of the night, when slow-wave sleep is most prominent.

**References**


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A 58-year-old man comes to the emergency department with a 1-day history of fever, headache, and vomiting. He underwent kidney transplantation last year. His temperature is 39.4 C (103 F), blood pressure is 130/80 mm Hg, pulse is 98/min, and respirations are 16/min. Neck stiffness is present on physical examination. Cerebrospinal fluid (CSF) results are as follows:

| | |
|---|---|
| Glucose | 40 mg/dL |
| Protein | 80 mg/dL |
| Leukocytes | 900/mm$^3$ |
| Neutrophils | 80% |

Gram-positive rods with tumbling motility at room temperature are seen on CSF microscopy. How was this patient's infection most likely transmitted?

A. Arthropod bite
B. Contaminated food
C. Needlestick


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| | |
|---|---|
| Protein | 80 mg/dL |
| Leukocytes | 900/mm$^3$ |
| Neutrophils | 80% |

Gram-positive rods with tumbling motility at room temperature are seen on CSF microscopy. How was this patient's infection most likely transmitted?

A. Arthropod bite
B. Contaminated food
C. Needlestick
D. Respiratory droplets
E. Unprotected sex

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| | |
|---|---|
| Protein | 80 mg/dL |
| Leukocytes | 900/mm$^3$ |
| Neutrophils | 80% |

Gram-positive rods with tumbling motility at room temperature are seen on CSF microscopy. How was this patient's infection most likely transmitted?

- A. Arthropod bite (1%)
- B. Contaminated food (72%)
- C. Needlestick (1%)
- D. Respiratory droplets (21%)
- E. Unprotected sex (2%)

Incorrect
Correct answer

72%
Answered correctly

01 min, 20 secs
Time Spent

09/21/2020
Last Updated



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This patient, who is almost certainly taking anti-rejection immunosuppressants given his kidney transplantation, has fever, headache, neck stiffness, and cerebrospinal fluid (CSF) findings suggestive of bacterial meningitis. There is CSF pleocytosis (elevated leukocyte count) with left shift, elevated protein, and low-normal glucose (low CSF glucose is seen in most though not all bacterial meningitis cases); and bacteria are seen on CSF microscopy.

The microbiologic findings are consistent with ***Listeria monocytogenes*** infection; this is a facultative intracellular (grows within macrophages), gram-positive rod, with distinctive flagellar-based **tumbling motility** (typically seen at room temperature but not at human body temperatures). *Listeria* can **multiply in cold temperatures** (4-10 C [39.2-50 F]), a unique feature that allows it to grow well in refrigerated foods. Listeriosis most often occurs in **immunocompromised** adults (eg, renal transplantation, hematologic malignancy). The bacteria can access the bloodstream following ingestion of contaminated food (eg, **unpasteurized milk** and milk products, undercooked meats, unwashed raw vegetables) and cause meningitis, meningoencephalitis, or bacteremia. *Listeria* can also be transmitted transplacentally or via vaginal contact during delivery, causing neonatal meningitis. Ampicillin is the antibiotic of choice.

**(Choice A)** Among the diseases transmitted by arthropod bites are: leishmaniasis (sandfly bite), *Plasmodium*/malaria (*Anopheles* mosquito bite), Chagas disease (reduviid bug bite), and *Borrelia*


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**(Choice A)** Among the diseases transmitted by arthropod bites are: leishmaniasis (sandfly bite), *Plasmodium*/malaria (*Anopheles* mosquito bite), Chagas disease (reduviid bug bite), and *Borrelia burgdorferi*/Lyme disease (*Ixodes* tick bite).

**(Choice C)** Needlesticks can transmit HIV, hepatitis B and C, and other infections.

**(Choice D)** *Neisseria meningitidis, Haemophilus influenzae, Mycobacterium tuberculosis*, and many other organisms are transmitted via respiratory droplets. *Listeria* infections are not transmitted in this manner.

**(Choice E)** Unprotected sex is the mode of transmission of HIV, hepatitis B, gonorrhea, chlamydia, syphilis, human papillomavirus (a cause of cervical cancer), and others.

**Educational objective:**
Listeriosis is most commonly transmitted through food ingestions and can cause meningitis in immunocompromised adults. *Listeria* is a gram-positive rod with tumbling motility. It grows well in cold temperatures and can therefore contaminate refrigerated food.

**References**


- What is new in listeriosis?
- Listeria monocytogenes regulates flagellar motility gene expression through MogR, a transcriptional




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www.ncbi.nlm.nih.gov/pubmed/24822197

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A 65-year-old man is brought to the emergency department after he suddenly became unresponsive at home. On arrival, paramedics found him pulseless with ventricular fibrillation. After 10 minutes of cardiopulmonary resuscitation, the patient regains spontaneous circulation. In the hospital, he is intubated and placed on mechanical ventilation. His vitals remain stable. A therapeutic hypothermia protocol is initiated. After 72 hours following rewarming, he remains comatose with fixed and dilated pupils. There is no direct or consensual pupillary response to light. MRI of the brain reveals diffuse loss of grey-white matter differentiation with sulcal effacement. Damage to which of the following areas of the brain is the most likely cause of this patient's pupillary findings?

A. Medulla
B. Midbrain
C. Occipital lobe
D. Parietal lobe
E. Pons
F. Temporal lobe



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home. On arrival, paramedics found him pulseless with ventricular fibrillation. After 10 minutes of cardiopulmonary resuscitation, the patient regains spontaneous circulation. In the hospital, he is intubated and placed on mechanical ventilation. His vitals remain stable. A therapeutic hypothermia protocol is initiated. After 72 hours following rewarming, he remains comatose with fixed and dilated pupils. There is no direct or consensual pupillary response to light. MRI of the brain reveals diffuse loss of grey-white matter differentiation with sulcal effacement. Damage to which of the following areas of the brain is the most likely cause of this patient's pupillary findings?

A. Medulla
B. Midbrain
C. Occipital lobe
D. Parietal lobe
E. Pons
F. Temporal lobe
G. Thalamus



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and placed on mechanical ventilation. His vitals remain stable. A therapeutic hypothermia protocol is initiated. After 72 hours following rewarming, he remains comatose with fixed and dilated pupils. There is no direct or consensual pupillary response to light. MRI of the brain reveals diffuse loss of grey-white matter differentiation with sulcal effacement. Damage to which of the following areas of the brain is the most likely cause of this patient's pupillary findings?

- A. Medulla (5%)
- ✓ B. Midbrain (58%)
- C. Occipital lobe (12%)
- D. Parietal lobe (1%)
- ✗ E. Pons (14%)
- F. Temporal lobe (3%)
- G. Thalamus (3%)

Incorrect
Correct answer

58%

01 min, 09 secs

01/02/2021



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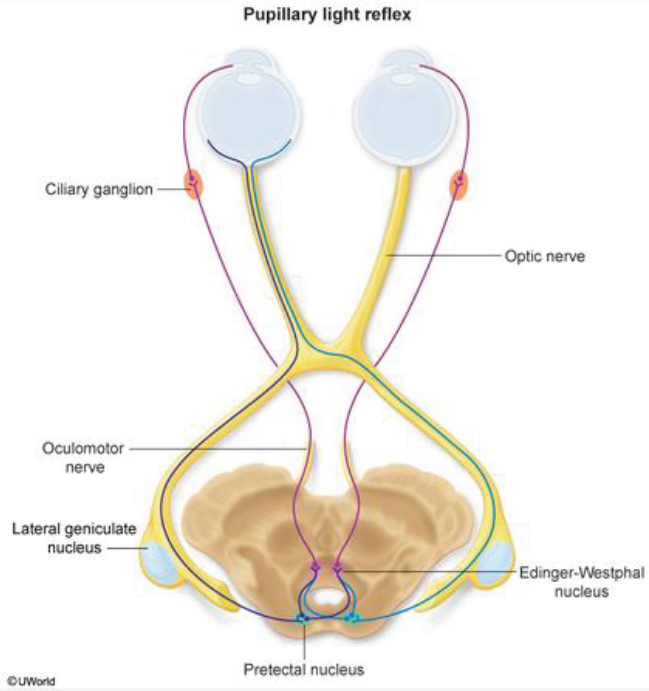


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This patient's presentation and MRI findings (eg, loss of grey-white matter differentiation with sulcal effacement) are consistent with anoxic brain injury due to cardiac arrest. The presence of nonreactive pupils to light stimulation following cardiac arrest carries a poor prognosis and indicates anoxic damage to the brainstem at the level of the **upper midbrain**.

During the normal **pupillary reflex**, the retina as well as the **optic nerve** and tract transmit the light stimulus to the midbrain at the level of the superior colliculus where it is received by the **pretectal nucleus** and subsequently relayed to the bilateral **Edinger-Westphal nuclei**. These nuclei subsequently project preganglionic parasympathetic fibers through the **oculomotor nerve** (CN III) to the ciliary ganglion, which then projects postganglionic fibers that innervate the sphincter pupillae muscle (constricts the pupil). When light is shone in one eye, both the ipsilateral pupil (direct response) and contralateral pupil (consensual response) constrict.

**(Choice A)** The medulla contains the glossopharyngeal (CN IX) and vagus (CN X) nerves, which provide the afferent and efferent limbs of the gag reflex, respectively.

**(Choice C)** The occipital lobe contains the primary visual cortex. Unilateral occipital lobe damage can cause contralateral homonymous hemianopia, whereas bilateral occipital lesions may result in cortical blindness.


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**(Choice D)** The parietal lobes process and interpret visual, auditory, and motor signals received from other brain areas. Parietal lobe damage results in difficulties with spatial and visual perception. Nondominant (eg, right-sided) lesions result in hemi-neglect and constructional apraxia, whereas dominant (eg, left-sided) lesions result in Gerstmann syndrome (eg, right-left confusion, agraphia, acalculia).

**(Choice E)** The pons contains the horizontal gaze center, which helps mediate the oculocephalic (doll's eye) reflex. It also contains the trigeminal (CN V) and facial (CN VII) nerves, which mediate the afferent and efferent limb of the corneal reflex, respectively. Bilateral pontine injury is associated with pinpoint pupils due to damage of the descending sympathetic fibers.

**(Choice F)** Temporal lobe injury can cause disturbances in memory (eg, hippocampus), speech (eg, Wernicke area in dominant hemisphere), vision (eg, Meyer loop), and hearing (eg, primary auditory cortex). Bilateral damage to the amygdala results in Klüver-Bucy syndrome (eg, hyperphagia, hyperorality, hypersexuality).

**(Choice G)** The thalamus is a major sensory relay station. The ventral posterolateral nucleus mediates somatic sensation of the body, the ventral posteromedial nucleus mediates facial sensation and taste, the lateral geniculate nucleus mediates vision, and the medial geniculate nucleus mediates hearing.

**Educational objective:**


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**(Choice F)** Temporal lobe injury can cause disturbances in memory (eg, hippocampus), speech (eg, Wernicke area in dominant hemisphere), vision (eg, Meyer loop), and hearing (eg, primary auditory cortex). Bilateral damage to the amygdala results in Klüver-Bucy syndrome (eg, hyperphagia, hyperorality, hypersexuality).

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**Educational objective:**
The upper midbrain contains neural structures (eg, optic nerve, pretectal nuclei, Edinger-Westphal nuclei, oculomotor nerve) that mediate the direct and consensual pupillary light reflex.

**References**

- The pupils.



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A 42-year-old man comes to the emergency department due to worsening jaw pain and stiffness. His symptoms began 2 days ago and have limited his ability to eat. Today the patient also developed painful stiffness in his neck. He has had no fever, chills, headache, focal weakness, or numbness. The patient is a farmer in rural Pennsylvania and sustained a wooden splinter injury to his forearm while working in a barn a week ago. He has no chronic medical conditions but has not had medical care for many years. On examination, the patient is not able to open his mouth. The muscles of the neck are tense, and neck range of motion is impaired. Which of the following is the best approach to establishing diagnosis in this patient?

- A. Anaerobic blood culture
- B. Cerebrospinal fluid analysis
- C. Clinical diagnosis only
- D. Serum toxin assay
- E. Several sets of antibody titers

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A. Anaerobic blood culture (8%)
B. Cerebrospinal fluid analysis (7%)
✓ C. Clinical diagnosis only (36%)
✗ D. Serum toxin assay (45%)
E. Several sets of antibody titers (2%)

Incorrect



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| Tetanus | |
|---|---|
| **Cause** | • ***Clostridium tetani*** spores inoculate skin wound → germinate → produce tetanus toxin → retrograde axonal transport to CNS → **blocks inhibitory interneurons**<br>• Risk: incomplete childhood vaccines or lack of 10-year booster shot |
| **Symptoms** | • **Trismus** (lockjaw) & difficulty swallowing<br>• Intermittent intense muscular spasms<br>• Opisthotonos (extremely arched back)<br>• Risus sardonicus (facial muscle spasm while smiling) |
| **Prevention** | • **Tetanus toxoid vaccination** |

**Tetanus** is rare in the developed world due to widespread vaccination with tetanus toxoid. However, cases can occur in individuals who were incompletely vaccinated as a child or those who **have not received booster vaccination** every 10 years (as is likely in this patient who has not been under medical care). The majority of patients who develop tetanus have a history of a **puncture wound** (eg, splinter) approximately


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**Tetanus** is rare in the developed world due to widespread vaccination with tetanus toxoid. However, cases can occur in individuals who were incompletely vaccinated as a child or those who **have not received booster vaccination** every 10 years (as is likely in this patient who has not been under medical care). The majority of patients who develop tetanus have a history of a **puncture wound** (eg, splinter) approximately a week prior to symptoms, which led to inoculation with *Clostridium tetani* spores. The spores germinate in anaerobic conditions into vegetative, rod-shaped bacteria and produce tetanus toxin (tetanospasmin). Tetanus toxin travels through lower motor neurons to the central nervous system where it inactivates inhibitory interneurons. Common manifestations include masseter muscle spasm (**lockjaw** [trismus]), muscle pain and stiffness, and difficulty swallowing.

Tetanus is a **clinical diagnosis** that should be suspected in patients who have characteristic symptoms, particularly if they are unlikely to be adequately vaccinated or have a history of recent cutaneous trauma. Blood cultures are not helpful because *C tetani* only grows at the inoculation site (the clinical syndrome stems from toxin elaboration not bacterial invasion) **(Choice A)**. Wound cultures can provide supportive evidence but often take several days to return, so they are not usually performed.

**(Choice B)** The neurologic manifestations of tetanus are caused by toxin-mediated blockade of inhibitory interneurons at the level of the anterior horn cells. Cerebrospinal fluid testing is usually normal and is not


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evidence but often take several days to return, so they are not usually performed.

**(Choice B)** The neurologic manifestations of tetanus are caused by toxin-mediated blockade of inhibitory interneurons at the level of the anterior horn cells. Cerebrospinal fluid testing is usually normal and is not typically part of diagnostic testing.

**(Choice D)** Serum tetanus toxin assay is not widely available and is not routinely used to diagnose tetanus. Tetanus is largely a clinical diagnosis.

**(Choice E)** Positive antitoxoid serology indicates that an individual is likely to be adequately vaccinated and reduces the chances that a patient has tetanus.

**Educational objective:**
Tetanus is a clinical diagnosis that should be suspected in patients who have characteristic symptoms (eg, lockjaw, muscle pain/spasms, difficulty swallowing), particularly if they are unlikely to be adequately vaccinated or have an antecedent cutaneous injury.

| Pathophysiology | Nervous System | Tetanus |
|---|---|---|
| Subject | System | Topic |

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A pharmaceutical researcher is developing a novel agent to prevent meningococcal disease in people exposed to the bacteria. Pili antigens from *Neisseria meningitidis* are extracted and used to generate monoclonal antibodies that impair normal pili function. The antibodies are administered to experimental animals with no prior exposure to *N meningitidis*. These animals, along with control animals that had not received the antibodies, are subsequently exposed to the bacteria. Compared to the control animals, a significantly greater proportion of the animals that received the antibodies remain healthy and develop no symptoms. The efficacy of these antibodies in preventing meningococcal disease is most likely due to direct interference with which of the following microbial processes?

A. Adhesion to vascular endothelial cells
B. Attachment to nasopharyngeal epithelial cells
C. Hematogenous dissemination
D. Invasion of the meninges
E. Survival inside phagocytes


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exposed to the bacteria. Pili antigens from *Neisseria meningitidis* are extracted and used to generate monoclonal antibodies that impair normal pili function. The antibodies are administered to experimental animals with no prior exposure to *N meningitidis*. These animals, along with control animals that had not received the antibodies, are subsequently exposed to the bacteria. Compared to the control animals, a significantly greater proportion of the animals that received the antibodies remain healthy and develop no symptoms. The efficacy of these antibodies in preventing meningococcal disease is most likely due to direct interference with which of the following microbial processes?

A. Adhesion to vascular endothelial cells (20%)
B. Attachment to nasopharyngeal epithelial cells (64%)
C. Hematogenous dissemination (4%)
D. Invasion of the meninges (6%)
E. Survival inside phagocytes (3%)

Correct

64%

01 min, 06 secs

09/25/2020



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***Neisseria meningitidis*** is commonly isolated from the oropharynx and nasopharynx of asymptomatic carriers. Colonization rates are variable but highest in close contact populations (eg, military recruits, university students). Transmission of meningococci usually occurs through exposure to respiratory droplets or direct contact with respiratory secretions. The **pili** on the capsular surface of *N meningitidis* are primarily responsible for attachment to and **colonization of the nasopharyngeal epithelium**. Pili also play a role in bacterial movement and epithelial penetration during invasion.

Pili undergo high rates of **antigenic variation** (due to on-off gene switching and horizontal gene transfer), which limits the effectiveness of vaccines against this target. Other prominent *N meningitidis* virulence factors include IgA protease (destroys mucosal antibodies that would otherwise inhibit epithelial colonization), capsular polysaccharides (prevent phagocytosis and phagolysosome destruction), lipo-oligosaccharide (an endotoxin that is the major source of toxicity), and Opa-proteins (aid in endothelial attachment and invasion).

**(Choices A and D)** *N meningitidis* penetration into the central nervous system is thought to occur at the cerebral capillary endothelial surface and, potentially, at the choroid plexus (the site of the blood–cerebrospinal fluid barrier). Vaccines that target endothelial or meningeal invasion would act too late in the disease process to prevent significant illness; once *N meningitidis* enters the circulatory system, increased


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oligosaccharide (an endotoxin that is the major source of toxicity), and Opa-proteins (aid in endothelial attachment and invasion).

**(Choices A and D)** *N meningitidis* penetration into the central nervous system is thought to occur at the cerebral capillary endothelial surface and, potentially, at the choroid plexus (the site of the blood–cerebrospinal fluid barrier). Vaccines that target endothelial or meningeal invasion would act too late in the disease process to prevent significant illness; once *N meningitidis* enters the circulatory system, increased levels of endotoxin put patients at high risk for sepsis, circulatory collapse, and death.

**(Choices C and E)** Most existing meningococcal vaccines target capsular polysaccharides. Capsular polysaccharides prevent phagocytosis and allow the pathogen to replicate and disseminate within the bloodstream. They also promote bacterial survival within phagocytes by inhibiting phagolysosome destruction.

**Educational objective:**
Pili are the primary virulence factor that allow *Neisseria meningitidis* to initially attach to and colonize the nasopharyngeal epithelial surface. Pili undergo significant antigenic variation, which makes them a difficult vaccination target.

**References**


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A 15-year-old girl is brought to the hospital due to sudden onset of severe left leg pain. She was practicing for an upcoming gymnastics competition when she felt a popping sensation after landing from a jump and developed anterior left leg pain. Following the injury, the patient was unable to bear weight on the leg. Physical examination shows swelling of the left knee with focal tenderness just above the patella. She is unable to raise the left leg against gravity while in the supine position. Imaging confirms a complete tear of the quadriceps tendon, but no fractures are identified. Surgical repair is planned. Lidocaine injection near which of the following sites is most likely to provide adequate anesthesia for the procedure?

A. Adductor canal
B. Inguinal ligament
C. Ischial spine tip
D. Medial tibial condyle
E. Obturator canal

Submit



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A 15-year-old girl is brought to the hospital due to sudden onset of severe left leg pain. She was practicing for an upcoming gymnastics competition when she felt a popping sensation after landing from a jump and developed anterior left leg pain. Following the injury, the patient was unable to bear weight on the leg. Physical examination shows swelling of the left knee with focal tenderness just above the patella. She is unable to raise the left leg against gravity while in the supine position. Imaging confirms a complete tear of the quadriceps tendon, but no fractures are identified. Surgical repair is planned. Lidocaine injection near which of the following sites is most likely to provide adequate anesthesia for the procedure?

A. Adductor canal (11%)
B. Inguinal ligament (53%)
C. ~~Ischial spine tip~~ (9%)
D. ~~Medial tibial condyle~~ (12%)
E. Obturator canal (13%)


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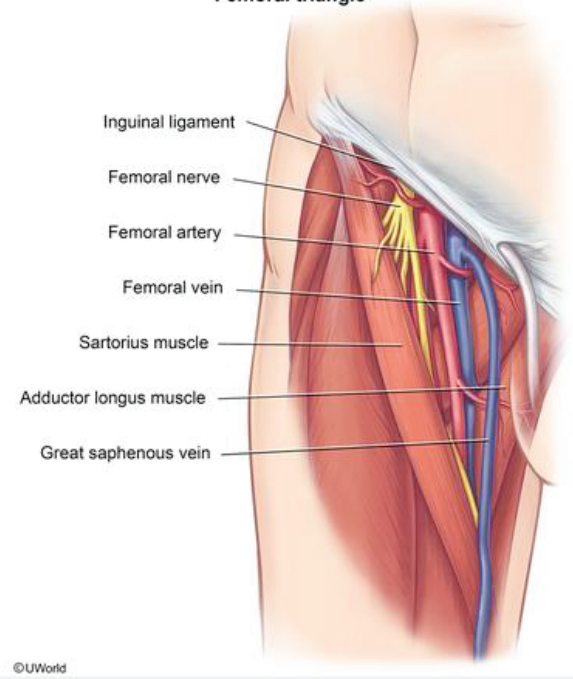
**Exhibit Display**

**Femoral triangle**

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The femoral nerve (L2-L4) innervates the quadriceps muscles (enabling extension at the knee and flexion at the hip) and provides sensation for the arch of the foot, shin, and anteromedial thigh. The nerve emerges between the psoas and iliacus muscles and passes under the **inguinal ligament** (lateral to the femoral artery) into the thigh before branching in the femoral triangle into an anterior and posterior division.

The optimal site for a **femoral nerve block** is right below the inguinal ligament (ie, in the inguinal crease) at the lateral border of the femoral artery. Injecting at this site **anesthetizes** the skin and muscles of the **anterior thigh, femur, and knee** and can be used during repair of the quadriceps tendon. The block also anesthetizes structures supplied by the saphenous nerve (ie, the terminal extension of the femoral nerve) to decrease sensation in the medial leg below the knee.

**(Choices A and D)** The saphenous nerve (a branch of the femoral nerve that supplies sensation to the leg) can be anesthetized directly at the level of the adductor canal in the thigh (ie, adductor canal block) or at the medial tibial condyle in the knee (ie, saphenous nerve block). However, the branches of the femoral nerve that supply the knee arise proximal to the saphenous nerve and would not be anesthetized by injection at these locations.

**(Choice C)** The ischial spine divides the greater and lesser sciatic foramina in the bony pelvis. The ischial



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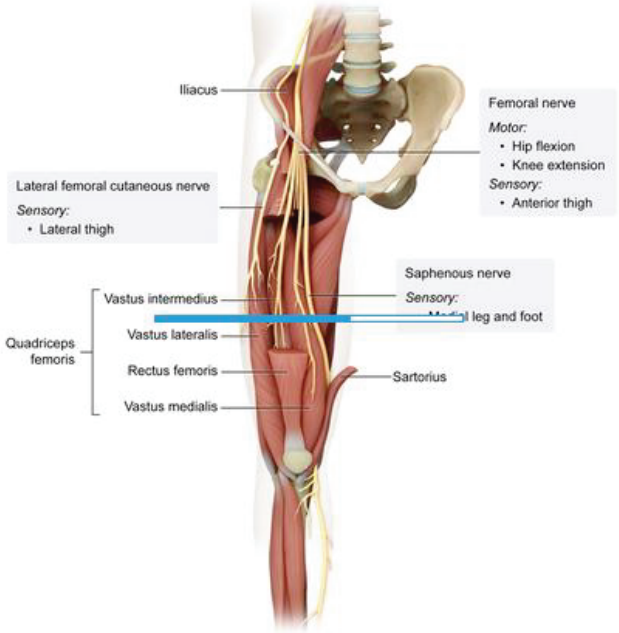
Femoral nerve and lateral femoral cutaneous nerve

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(Choice C) The ischial spine divides the greater and lesser sciatic foramina in the bony pelvis. The ischial



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nerve that supply the knee arise proximal to the saphenous nerve and would not be anesthetized by injection at these locations.

**(Choice C)** The ischial spine divides the greater and lesser sciatic foramina in the bony pelvis. The ischial spine tip is a landmark for pudendal nerve block, which is used for anesthesia during vaginal deliveries and for minor surgeries of the vagina and perineum.

**(Choice E)** The obturator canal is a small gap in the obturator membrane (ie, the fibrous sheet covering the obturator foramen) that allows the obturator artery, obturator vein, and obturator nerve to travel from the pelvis to the thigh. An obturator nerve block would anesthetize the adductor muscles of the thigh and the skin of the medial aspect of the thigh but would not affect the quadriceps muscles or sensation to the knee.

**Educational objective:**

A femoral nerve block below the inguinal ligament (ie, in the inguinal crease) will anesthetize the skin and muscles of the anterior thigh, femur, and knee. This type of block can be used in patients requiring tendon repair after a knee injury (eg, quadriceps rupture).

**References**

- Anatomical landmarks for femoral nerve block: a comparison of four needle insertion sites.



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nerve that supply the knee arise proximal to the saphenous nerve and would not be anesthetized by

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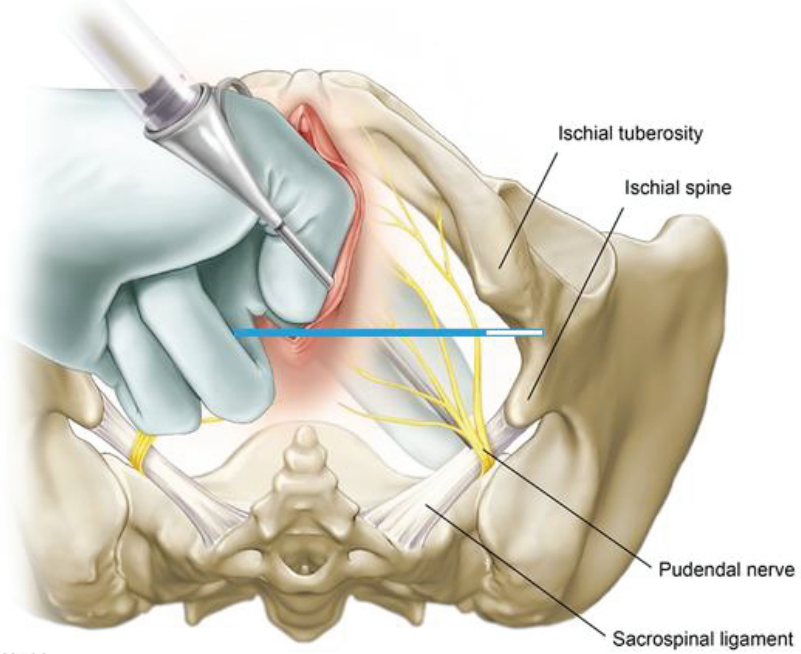
Pudendal nerve block

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A 64-year-old man comes to the office due to slowing of his movements and gait instability that has been the cause of several recent falls. The patient was diagnosed with Parkinson disease a year ago. On examination, there is a resting tremor involving the right hand and rigidity during passive flexion and extension of the right upper limb. The patient is started on therapy with pramipexole. Which of the following best describes the mechanism of action of this medication?

A. Decreases central dopamine degradation
B. Directly stimulates dopamine receptors
C. Enhances the effect of endogenous dopamine
D. Increases dopamine precursor availability in the brain
E. Inhibits central muscarinic receptors

Submit



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A 64-year-old man comes to the office due to slowing of his movements and gait instability that has been the cause of several recent falls. The patient was diagnosed with Parkinson disease a year ago. On examination, there is a resting tremor involving the right hand and rigidity during passive flexion and extension of the right upper limb. The patient is started on therapy with pramipexole. Which of the following best describes the mechanism of action of this medication?

A. Decreases central dopamine degradation (15%)

✓ B. Directly stimulates dopamine receptors (50%)

C. Enhances the effect of endogenous dopamine (14%)

D. Increases dopamine precursor availability in the brain (10%)

E. Inhibits central muscarinic receptors (9%)

Correct

50%
Answered correctly

53 secs
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02/05/2021
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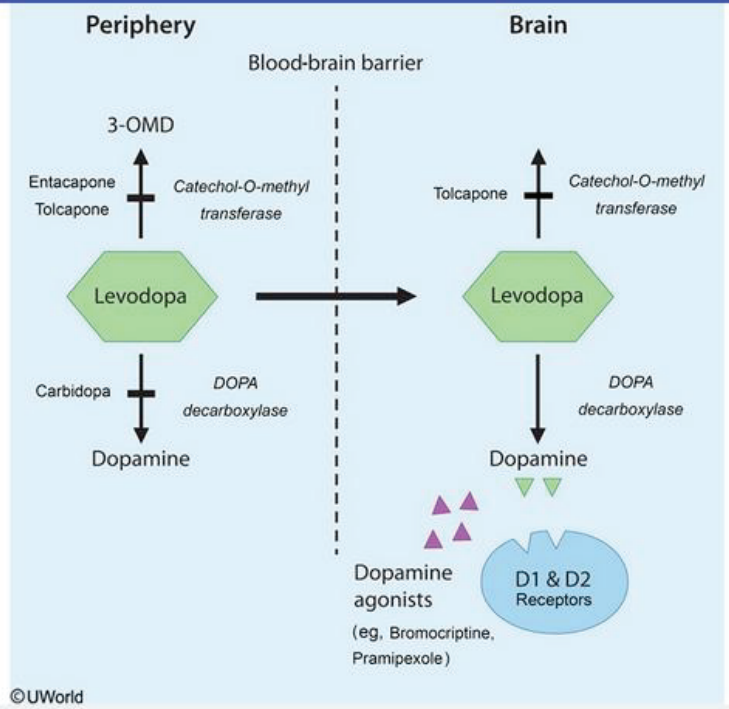


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**Dopamine agonists** have a chemical structure similar to the neurotransmitter dopamine and directly stimulate dopamine receptors. They do not have to be metabolized to be active. There are 2 classes of dopamine agonists:

- Ergot compounds (derived from ergot fungi): **bromocriptine**
- Nonergot compounds: **pramipexole** and **ropinirole**

Dopamine agonists have an important role in the treatment of **Parkinson disease** (PD) as these medications have a long half-life and can delay the need to start levodopa, thereby postponing the development of motor fluctuations until later in the disease course. Bromocriptine also treats hyperprolactinemia.

**(Choice A)** Selegiline is used to delay the clinical progression of PD via inhibition of monoamine oxidase-B (MAO-B) in the brain, resulting in decreased central dopamine degradation.

**(Choice C)** Amantadine exerts several effects with regard to PD. As an indirect and direct dopaminergic agent, it alleviates some of the motor symptoms of PD by enhancing the effects of endogenous dopamine. It is thought also to have some anticholinergic properties, which reduce tremors.

**(Choice D)** Both catechol-O-methyltransferase (COMT) inhibitors (eg, entacapone, tolcapone) and dopa


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**(Choice C)** Amantadine exerts several effects with regard to PD. As an indirect and direct dopaminergic agent, it alleviates some of the motor symptoms of PD by enhancing the effects of endogenous dopamine. It is thought also to have some anticholinergic properties, which reduce tremors.

**(Choice D)** Both catechol-O-methyltransferase (COMT) inhibitors (eg, entacapone, tolcapone) and dopa decarboxylase inhibitors (eg, carbidopa) decrease the breakdown of levodopa in peripheral tissues and increase the amount of levodopa available to cross the blood-brain barrier.

**(Choice E)** Anticholinergics, such as trihexyphenidyl and benztropine, inhibit central muscarinic receptors. These drugs are sometimes used to treat patients with drug-induced parkinsonism and those with tremor as the predominant symptom of idiopathic PD.

**Educational objective:**

Dopamine agonists have a chemical structure similar to the neurotransmitter dopamine and directly stimulate dopamine receptors. The 2 classes of dopamine agonists are ergot compounds (eg, bromocriptine) and nonergot compounds (eg, pramipexole, ropinirole).

**References**

- Current pharmacotherapeutic treatment options in Parkinson's disease.
- Parkinson's disease: diagnosis and treatment



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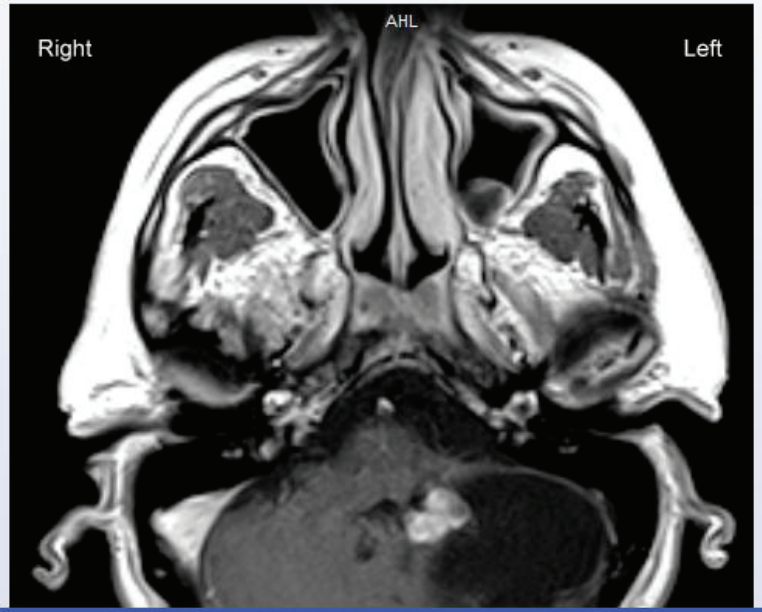
A 55-year-old man comes to the office due to progressive headaches over the past 2 months. The headaches are throbbing, often associated with nausea, and worsen whenever the patient coughs or bears down during a bowel movement. Medical history is significant for episodic migraine without aura. MRI of the brain with gadolinium reveals a cystic mass, as shown in the image below:



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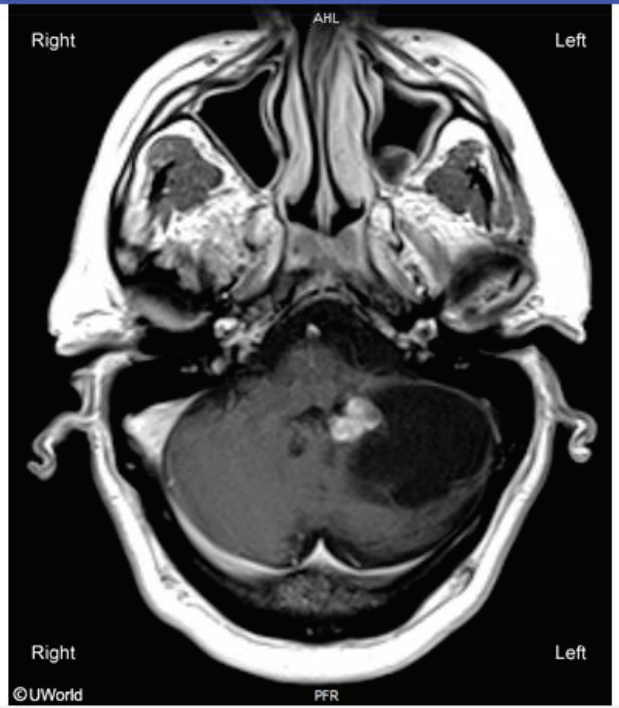


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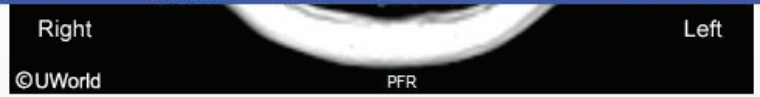


Which of the following findings is most likely to be seen on physical examination of this patient?

- A. Left dysdiadochokinesia
- B. Left Horner syndrome
- C. Left oculomotor nerve palsy
- D. Photophobia
- E. Right hemiparesis
- F. Right hemisensory loss
- G. Right homonymous hemianopia
- H. Right lower facial droop

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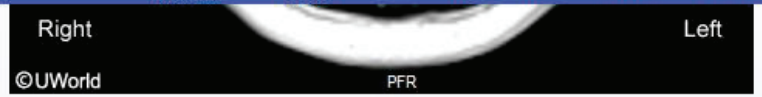


Which of the following findings is most likely to be seen on physical examination of this patient?

- A. Left dysdiadochokinesia (66%)
- B. ~~Left Horner syndrome~~ (3%)
- C. ~~Left oculomotor nerve palsy~~ (4%)
- D. ~~Photophobia~~ (1%)
- E. ~~Right hemiparesis~~ (8%)
- F. ~~Right hemisensory loss~~ (3%)
- G. ~~Right homonymous hemianopia~~ (8%)
- H. ~~Right lower facial droop~~ (3%)

Correct

66%

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01/03/2021



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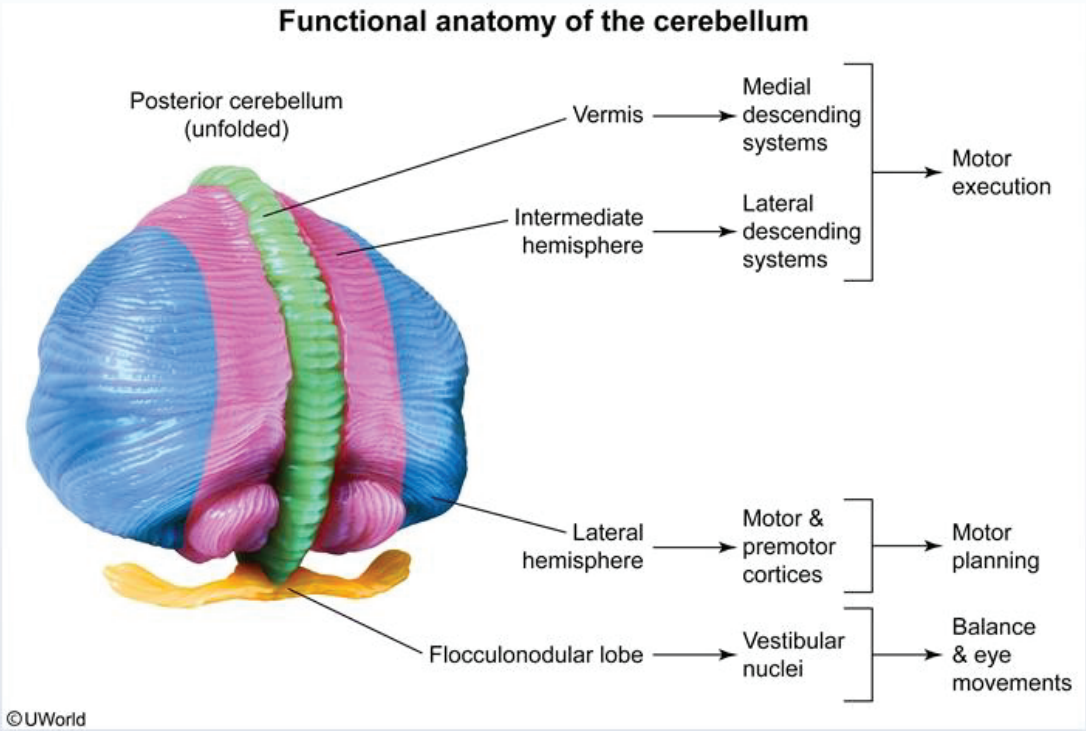


This patient has an expanding cystic neoplasm (likely a hemangioblastoma) in the **left cerebellar hemisphere** causing progressive headaches that worsen with Valsalva (maneuver increases intracranial



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This patient has an expanding cystic neoplasm (likely a hemangioblastoma) in the **left cerebellar hemisphere** causing progressive headaches that worsen with Valsalva (maneuver increases intracranial pressure).

The cerebellum is the largest structure in the posterior fossa and consists of the vermis at the midline and 2 cerebellar hemispheres. The cerebellar hemispheres are primarily responsible for motor planning and **coordination** of the **ipsilateral extremities** via their connections with the lateral descending motor systems (eg, lateral corticospinal tract, rubrospinal tract). Consequently, lesions affecting the left cerebellar hemisphere typically result in **left dysdiadochokinesia** (impaired rapid alternating movements), limb dysmetria (overshoot/undershoot during targeted movement), and **intention tremor** (tremor during targeted movement).

The cerebellar vermis modulates axial/truncal posture and coordination via connections with the medial descending motor systems (eg, anterior corticospinal, reticulospinal, vestibulospinal, and tectospinal tracts). Lesions to this region result in truncal ataxia (eg, wide-based, unsteady gait). Vertigo and nystagmus may also occur due to disruption of the inferior vermis and the flocculonodular lobe.

**(Choice B)** Horner syndrome (eg, partial ptosis, miosis, anhidrosis) is associated with lesions affecting the



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nystagmus may also occur due to disruption of the inferior vermis and the flocculonodular lobe.

**(Choice B)** Horner syndrome (eg, partial ptosis, miosis, anhidrosis) is associated with lesions affecting the ipsilateral lateral hypothalamus or sympathetic tracts in the brainstem (eg, lateral medulla, carotid artery).

**(Choice C)** Oculomotor nerve palsy (mydriasis, complete ptosis, and "down and out" deviation of the eye) may occur with an ipsilateral lesion at the level of the anterior midbrain or midbrain tegmentum.

**(Choice D)** Acute migraine is characterized by throbbing unilateral headache associated with nausea/vomiting, phonophobia, and photophobia. Migraine is unlikely in this patient as his headache worsens with Valsalva (suggestive of increased intracranial pressure) and neuroimaging shows a cerebellar mass.

**(Choices E, F, and H)** Contralateral hemiparesis, hemisensory loss, and/or lower facial droop can occur with cortical, subcortical, or upper brainstem lesions.

**(Choice G)** A unilateral visual pathway lesion beyond the optic chiasm (eg, optic tract, lateral geniculate body, optic radiations, primary visual cortex) can cause contralateral homonymous hemianopia.

**Educational objective:**
The cerebellar hemispheres are responsible for motor planning and coordination of the ipsilateral


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**(Choice D)** Acute migraine is characterized by throbbing unilateral headache associated with nausea/vomiting, phonophobia, and photophobia. Migraine is unlikely in this patient as his headache worsens with Valsalva (suggestive of increased intracranial pressure) and neuroimaging shows a cerebellar mass.

**(Choices E, F, and H)** Contralateral hemiparesis, hemisensory loss, and/or lower facial droop can occur with cortical, subcortical, or upper brainstem lesions.

**(Choice G)** A unilateral visual pathway lesion beyond the optic chiasm (eg, optic tract, lateral geniculate body, optic radiations, primary visual cortex) can cause contralateral homonymous hemianopia.

**Educational objective:**

The cerebellar hemispheres are responsible for motor planning and coordination of the ipsilateral extremities via their connections with the lateral descending motor systems. Consequently, cerebellar hemisphere lesions typically result in ipsilateral dysdiadochokinesia, limb dysmetria, and/or intention tremor.

**References**

- Lesion-symptom mapping of the human cerebellum.


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A 55-year-old woman is brought to the office by her husband for evaluation of strange behavior. She has been spending large amounts of money to buy expensive clothes and jewelry. The patient has also offered sex to unknown men in the neighborhood and has become increasingly indifferent toward her family, about whom she used to care deeply. She usually drinks 1 or 2 glasses of wine on weekends but lately has been drinking 2 or 3 glasses almost every day. When asked about these changes during the interview, the patient states that she has not noticed any change in her behavior. Vital signs are normal. The general physical and neurologic examinations are normal. This patient's condition is most likely due to abnormal accumulation of which of the following?

A. Ataxin
B. Beta-amyloid
C. Polyglutamine
D. Prions
E. Ubiquitinated TDP-43



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- A. Ataxin (2%)
- ✗ B. Beta-amyloid (15%)
- C. Polyglutamine (15%)
- D. Prions (14%)
- ✓ E. Ubiquitinated TDP-43 (52%)

Incorrect
Correct answer

52%
Answered correctly

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Time Spent

12/20/2020
Last Updated



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This patient with disinhibition (eg, soliciting sex from strangers), loss of empathy toward her family, complex compulsive behaviors (eg, excessive shopping), and hyperorality (eg, increase in drinking wine) likely has **frontotemporal dementia** (FTD). FTD is characterized by degeneration of the prefrontal cortex, which progresses to include the anterior temporal lobes. The disease process results in accumulation of different **neurotoxic proteins**, including:

- **Tau**, a protein associated with neuronal microtubules that normally takes part in microtubule stabilization. In patients with FTD, tau becomes **hyperphosphorylated** and disassociates from the microtubules, which may lead to instability and disrupted axonal transport. It also forms paired helical filaments, which create intracellular tangled clumps of tau proteins predominantly in the frontal and temporal lobes, as well as the hippocampi. Tau-related neurofibrillary tangles are also found in patients with Alzheimer dementia.
- **TDP-43** (transactive response DNA-binding protein 43), a protein that normally functions as a transcription inhibitor or a DNA repair protein. **Abnormal ubiquitination** leads to immunoreactive inclusions of TDP-43. Pathologic TDP-43 is also found in patients with amyotrophic lateral sclerosis.

**(Choices A and C)** CAG trinucleotide (polyglutamine) repeats can lead to neurotoxic protein formation. When this occurs in the ataxin genes, it can lead to spinocerebellar ataxia. When it occurs in the huntingtin


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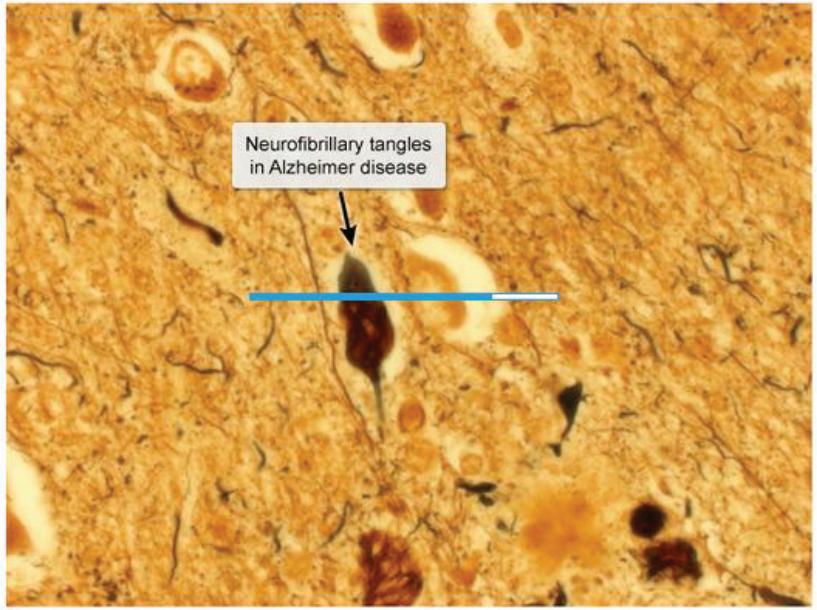
Exhibit Display

Alzheimer disease

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which this occurs in the ataxin genes, it can lead to spinocerebellar ataxia. When it occurs in the huntingtin



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inclusions of TDP-43. Pathologic TDP-43 is also found in patients with amyotrophic lateral sclerosis.

**(Choices A and C)** CAG trinucleotide (polyglutamine) repeats can lead to neurotoxic protein formation. When this occurs in the ataxin genes, it can lead to spinocerebellar ataxia. When it occurs in the huntingtin protein, it leads to Huntington disease, which can present with prominent changes in mood or cognition. However, both spinocerebellar ataxia and Huntington disease also typically present with significant gait abnormalities (ie, ataxia).

**(Choice B)** Extracellular accumulation of beta-amyloid occurs in Alzheimer disease. Alzheimer disease commonly presents with early and prominent memory impairment with language deficits and spatial disorientation. Although personality changes can occur, they typically occur later in the disease process. This patient's early personality changes are more characteristic of FTD.

**(Choice D)** Excessive prion accumulation causes Creutzfeldt-Jakob disease. Although behavioral changes are common, dementia is rapidly progressive and associated with myoclonus and/or seizures.

**Educational objective:**
Frontotemporal dementia presents with early personality change, executive dysfunction, compulsivity, and hyperorality. It is associated with neurofibrillary tangles due to abnormal tau proteins (also seen in Alzheimer dementia) and pathologically ubiquitinated TDP-43 (also seen in amyotrophic lateral sclerosis).


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A 6-year-old boy is brought to the office by his mother due to difficulty with his behavior in school. She says that his teacher is concerned that he does not pay attention in class and his grades are dropping to the point he may need medication to help him focus. The patient's mother has noticed that at home he seems to stare into space for several seconds, multiple times throughout the day. This occurs even when he is watching his favorite television show, and he seems to ignore her when she calls his name. The patient has no previous medical problems and takes no medications. He has an older brother with attention-deficit hyperactivity disorder and an aunt with epilepsy. Which of the following is the most appropriate pharmacotherapy for this patient?

A. Carbamazepine
B. Ethosuximide
C. Lorazepam
D. Methylphenidate
E. Phenobarbital


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says that his teacher is concerned that he does not pay attention in class and his grades are dropping to the point he may need medication to help him focus. The patient's mother has noticed that at home he seems to stare into space for several seconds, multiple times throughout the day. This occurs even when he is watching his favorite television show, and he seems to ignore her when she calls his name. The patient has no previous medical problems and takes no medications. He has an older brother with attention-deficit hyperactivity disorder and an aunt with epilepsy. Which of the following is the most appropriate pharmacotherapy for this patient?

A. Carbamazepine (2%)
B. Ethosuximide (83%)
C. Lorazepam (0%)
D. Methylphenidate (11%)
E. Phenobarbital (1%)

Correct

83%
Answered correctly

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| Absence seizures | |
|---|---|
| **Clinical features** | • Sudden impairment of consciousness ("staring spells")<br>• Preserved muscle tone<br>• Unresponsive to tactile/verbal stimulation<br>• Short duration (<20 sec)<br>• Simple automatisms frequently present<br>• Easily provoked by hyperventilation |
| **Diagnosis** | EEG: 3-Hz spike-wave discharges during episodes |
| **Treatment** | Ethosuximide |

**EEG** = electroencephalogram.

**Absence seizures**, a type of **generalized** epilepsy, present in children age 4-10 as brief **staring spells** with a momentary lapse in consciousness. Automatisms, such as rhythmic blinking or repetitive lip smacking, may occur. Most absence seizures last approximately 10 seconds, and behavior and awareness typically return immediately to normal following an attack. The patient experiences **no**


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**postictal** period and usually has no recollection that a seizure has occurred. Absence seizures are characteristically provoked by **hyperventilation**, and electroencephalogram will show generalized **3-Hz spike-wave** complexes.

Treatment of absence seizures is typically with **ethosuximide**, which inhibits T-type calcium channels in thalamic neurons. Valproate can also be used if first-line therapy is not tolerated or ineffective. Childhood absence epilepsy is typically benign, and seizures often resolve before puberty.

**(Choices A and E)** Narrow-spectrum anticonvulsants (eg, carbamazepine, gabapentin, phenobarbital, phenytoin) are generally favored for focal-onset seizures. Carbamazepine can worsen absence seizures and phenobarbital is ineffective in these patients.

**(Choice C)** Lorazepam is a benzodiazepine that is used as a first-line anticonvulsant in a patient with status epilepticus.

**(Choice D)** Methylphenidate is an indirect-acting sympathomimetic used to treat attention-deficit hyperactivity disorder (ADHD). Although ADHD may present similarly with "inattention," staring episodes consistent with absence seizures do not occur out of boredom or lack of focus and cannot be interrupted by verbal/tactile stimuli.


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**(Choice C)** Lorazepam is a benzodiazepine that is used as a first-line anticonvulsant in a patient with status epilepticus.

**(Choice D)** Methylphenidate is an indirect-acting sympathomimetic used to treat attention-deficit hyperactivity disorder (ADHD). Although ADHD may present similarly with "inattention," staring episodes consistent with absence seizures do not occur out of boredom or lack of focus and cannot be interrupted by verbal/tactile stimuli.

**Educational objective:**

Absence seizures are a type of generalized epilepsy characterized by brief staring spells with momentary loss of awareness followed by an abrupt return to full consciousness. A classic 3-Hz spike-wave is seen on electroencephalogram; the treatment is ethosuximide.

**References**

- Ethosuximide, sodium valproate or lamotrigine for absence seizures in children and adolescents.

| Pharmacology | Nervous System | Seizures |
| --- | --- | --- |
| Subject | System | Topic |



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A 25-year-old man is brought to the emergency department after being found unresponsive. He has a history of schizoaffective disorder and previous suicide attempts by prescription medication overdose. The patient was recently started on haloperidol and sertraline. Temperature is 40.6 C (105 F), blood pressure is 180/98 mm Hg, and pulse is 112/min. On examination, the patient is obtunded and diffusely rigid without clonus. Laboratory studies show serum creatinine of 3.2 mg/dL, creatine kinase of 75,000 U/L, and leukocytes of 16,000/mm$^3$. The antidote for this patient's current condition most likely has which of the following mechanisms of action?

A. Activation of presynaptic voltage-gated calcium channels of motor neurons

B. Antagonism of peripheral and central serotonin receptors

C. Blockade of central dopamine D2 receptors

D. Inhibition of acetylcholinesterase at the neuromuscular junction

E. Inhibition of calcium ion release from sarcoplasmic reticulum of skeletal muscle

Submit



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A. Activation of presynaptic voltage-gated calcium channels of motor neurons (3%)

B. Antagonism of peripheral and central serotonin receptors (19%)

C. Blockade of central dopamine D2 receptors (10%)

D. Inhibition of acetylcholinesterase at the neuromuscular junction (6%)

✓ E. Inhibition of calcium ion release from sarcoplasmic reticulum of skeletal muscle (60%)



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| Neuroleptic malignant syndrome | |
|---|---|
| **Signs/symptoms** | • Fever (>40 C common)<br>• Confusion<br>• Muscle rigidity (generalized)<br>• Autonomic instability (abnormal vital signs, sweating) |
| **Treatment** | • Stop antipsychotics or restart dopamine agents<br>• Supportive care (hydration, cooling), intensive care unit<br>• Dantrolene or bromocriptine if refractory |

This patient has **neuroleptic malignant syndrome** (NMS) likely caused by an overdose of haloperidol. NMS is a life-threatening adverse reaction most commonly resulting from the use of **antipsychotics** (neuroleptic) medications, which block dopamine receptors in the brain. NMS presents clinically with **diffuse muscle rigidity, high fever, autonomic instability** (hypertension, tachycardia), and altered


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**diffuse muscle rigidity**, **high fever**, **autonomic instability** (hypertension, tachycardia), and altered sensorium. Laboratory findings include **creatine kinase elevation** due to rhabdomyolysis, which can result in acute renal failure.

The mainstay of treatment is to discontinue the causative agent and provide supportive care (eg, intravenous hydration). In severe cases, **dantrolene** can be administered, which antagonizes ryanodine receptors and inhibits calcium release from the sarcoplasmic reticulum. Bromocriptine, a dopamine agonist, has also shown clinical benefit in NMS.

**(Choice A)** Activation of presynaptic voltage-gated calcium channels at the neuromuscular junction will trigger calcium influx into the terminal bulb. This will increase the release of acetylcholine from the terminal bulb onto the muscle endplate and, therefore, promote skeletal muscle contraction.

**(Choice B)** Serotonin receptor antagonists (eg, cyproheptadine) can be used to treat serotonin syndrome. Similar to NMS, serotonin syndrome can present with altered mental status and autonomic instability (diaphoresis, hypertension, hyperthermia, tachycardia). However, serotonin syndrome commonly presents with *hyperreflexia and myoclonus* (not diffuse rigidity) and gastrointestinal symptoms (nausea, diarrhea, vomiting).

**(Choice C)** Blockade of central dopamine D2 receptors in the brain leads to the extrapyramidal symptoms


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Similar to NMS, serotonin syndrome can present with altered mental status and autonomic instability (diaphoresis, hypertension, hyperthermia, tachycardia). However, serotonin syndrome commonly presents with *hyperreflexia and myoclonus* (not diffuse rigidity) and gastrointestinal symptoms (nausea, diarrhea, vomiting).

**(Choice C)** Blockade of central dopamine D2 receptors in the brain leads to the extrapyramidal symptoms (eg, diffuse rigidity) observed in NMS.

**(Choice D)** Inhibition of acetylcholinesterase results in increased acetylcholine at the neuromuscular junction, promoting skeletal muscle activation and contraction. Procholinergic agents should be avoided in NMS as they may exacerbate symptoms.

**Educational objective:**

Neuroleptic malignant syndrome is a life-threatening reaction to antipsychotic medications characterized by diffuse muscle rigidity, hyperthermia, autonomic instability, and altered sensorium. The antipsychotic should be stopped and supportive care provided; dantrolene, a ryanodine receptor blocker that inhibits calcium release from the sarcoplasmic reticulum, is an effective antidote.

**References**

- Neuroleptic malignant syndrome: a neuro-psychiatric emergency: recognition, prevention, and



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A 52-year-old woman comes to the office due to a hand tremor that has been present for several months. It is most prominent while she is carrying out simple daily activities such as drinking from a glass or pouring from a tea kettle. When asked if anything improves the tremor, the patient mentions that it subsides somewhat when she drinks small amounts of alcohol. Family history is significant for similar problems in her mother. Vital signs are normal. Neurologic examination shows bilateral tremor in the upper extremities. Which of the following is the best treatment for this patient?

A. Benztropine
B. Clozapine
C. Diazepam
D. Haloperidol
E. L-DOPA
F. Propranolol

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A. Benztropine (12%)
B. Clozapine (2%)
C. Diazepam (19%)
D. Haloperidol (1%)
E. L-DOPA (12%)
F. Propranolol (52%)



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This patient has **essential tremor**, the most commonly diagnosed movement disorder. Essential tremor is also referred to as **familial** tremor as it often follows **autosomal dominant** inheritance. A positive family history of tremor can sometimes assist in making the diagnosis. Essential tremor classically worsens while maintaining a particular posture (eg, when holding an object). Patients commonly report that their symptoms **improve with alcohol consumption**. **Propranolol** is the first-line treatment for essential tremor. This nonselective β-adrenergic antagonist is thought to lessen the tremor via central nervous system effects.

**(Choice A)** Benztropine is an anticholinergic agent that can be used to treat tremor in Parkinson disease and to counteract the extrapyramidal side effects of neuroleptic medications such as haloperidol.

**(Choices B and D)** Haloperidol is most commonly used to treat the positive symptoms of psychosis (eg, delusions, hallucinations). Clozapine is an atypical antipsychotic that blocks $D_2$ (dopamine) and $5HT_2$ (serotonin) receptors in the CNS.

**(Choice C)** Diazepam is a benzodiazepine that is effective for treatment of seizures and alcohol withdrawal. This patient has had intention tremor for several months and family history is positive for essential tremor; these findings would make alcohol withdrawal very unlikely.


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**(Choices B and D)** Haloperidol is most commonly used to treat the positive symptoms of psychosis (eg, delusions, hallucinations). Clozapine is an atypical antipsychotic that blocks $D_2$ (dopamine) and $5HT_2$ (serotonin) receptors in the CNS.

**(Choice C)** Diazepam is a benzodiazepine that is effective for treatment of seizures and alcohol withdrawal. This patient has had intention tremor for several months and family history is positive for essential tremor; these findings would make alcohol withdrawal very unlikely.

**(Choice E)** L-DOPA, or levodopa, is used in combination with the DOPA decarboxylase inhibitor carbidopa to treat Parkinson disease. Patients with Parkinson disease have a resting tremor.

**Educational objective:**
Essential tremor is the most common movement disorder. Patients experience a slowly progressive, symmetric postural and/or kinetic tremor that most commonly affects the upper extremities. Essential tremor is often inherited in an autosomal dominant fashion (referred to as familial tremor). First-line treatment is the nonspecific β-adrenergic antagonist propranolol.

| Pharmacology | Nervous System | Tremor |
|---|---|---|
| Subject | System | Topic |



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A 3-year-old boy is rushed to the emergency department after he is found underwater in the bathtub. His parents say the patient was left alone for 5 minutes. On physical examination, he does not respond to painful stimuli and is pulseless and not breathing. Cardiac rhythm is asystole and spontaneously returns after several minutes of resuscitation. While performing endotracheal intubation, stimulation of the posterior pharyngeal wall with laryngoscope elicits no soft palate movements or gagging. This patient's findings during intubation most likely indicate dysfunction of which of the following neural structures?

A. Prefrontal cortex
B. Motor cortex
C. Midbrain
D. Medulla oblongata
E. Cervical spinal cord

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A. Prefrontal cortex (1%)
B. Motor cortex (3%)
C. Midbrain (12%)
D. Medulla oblongata (79%)
E. Cervical spinal cord (3%)

Correct

79%
Answered correctly

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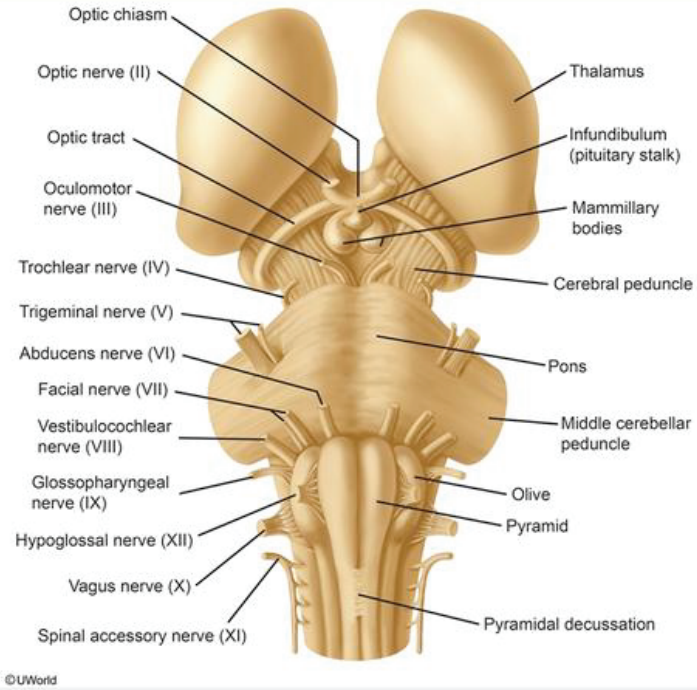


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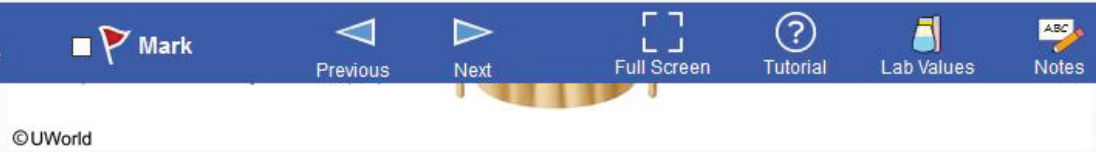

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This patient with prolonged oxygen deprivation has an **absent gag reflex**. The gag reflex is an airway protective mechanism that acts to expel foreign or toxic material from the aerodigestive tract. It is mediated by the following:

- Sensory (afferent) signals from the back of the tongue or posterior pharyngeal wall are sent via the **glossopharyngeal nerve** (CN IX).
- Somatic sensory fibers of CN IX **enter the brainstem at the medulla**, descend along the spinal trigeminal tract, and synapse in the caudal spinal nucleus.
- Information is then sent to the **bilateral nuclei ambiguus**, which are also located in the medulla.
- Bilateral motor (efferent) signals are sent via the **vagus nerves** (CN X), causing elevation of the soft palate and contraction of the pharynx.

Therefore, an absent gag reflex is suspicious for dysfunction of the **medulla oblongata**. In combination with a prolonged anoxic period, this is concerning for **brain death**, which is the irreversible absence of cerebral and brainstem reflexes.

**(Choice A)** Damage to the prefrontal cortex can cause inappropriate behavior, impaired judgment, and



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**(Choice A)** Damage to the prefrontal cortex can cause inappropriate behavior, impaired judgment, and poor problem-solving skills (ie, executive dysfunction). It cannot be evaluated in an unconscious patient.

**(Choice B)** The motor cortex is responsible for generating voluntary motor movement and cannot be tested in an unconscious patient. The gag reflex is involuntary and mediated by cranial nerves in the medulla.

**(Choice C)** The pupillary reflex is also assessed in patients with suspected brain death and indicates dysfunction of the midbrain. It is mediated by afferents from the optic nerve (CN II) and efferents from the oculomotor nerve (CN III) to mediate constriction of the pupils in response to light.

**(Choice E)** The cervical spinal cord can mediate several reflexes including neck flexion, adduction of the shoulders, elbow flexion, and flexion of the trunk. These may even be present in patients with brain death. However, the gag reflex is mediated by cranial (rather than spinal) nerves.

**Educational objective:**
The gag reflex is mediated by afferents predominantly from the glossopharyngeal nerve (CN IX) and efferents from the vagus nerve (CN X). An absent gag reflex may indicate dysfunction of the medulla oblongata, where the involved cranial nerve nuclei reside.


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A 35-year-old woman with a history of migraines is evaluated due to a recent increase in headache frequency and severity. She has had no focal weakness, sensory loss, vision changes, or seizures. The patient has no other medical conditions and takes sumatriptan as needed. She does not use tobacco, alcohol, or illicit drugs. Physical examination shows no focal neurological deficits. Neuroimaging reveals a small aneurysm arising from the segment of right internal carotid artery within the cavernous sinus. If this patient's aneurysm continues to expand, which of the following findings is most likely to be observed?

A. Deviation of the tongue to the right when protruded
B. Inability to contract the right orbicularis oculi muscle
C. Loss of sensation from anterior two-thirds of the tongue
D. Vision defect affecting the left half of the visual field
E. Weakness of the right lateral rectus muscle

Submit



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A 35-year-old woman with a history of migraines is evaluated due to a recent increase in headache frequency and severity. She has had no focal weakness, sensory loss, vision changes, or seizures. The patient has no other medical conditions and takes sumatriptan as needed. She does not use tobacco, alcohol, or illicit drugs. Physical examination shows no focal neurological deficits. Neuroimaging reveals a small aneurysm arising from the segment of right internal carotid artery within the cavernous sinus. If this patient's aneurysm continues to expand, which of the following findings is most likely to be observed?

A. Deviation of the tongue to the right when protruded (2%)
B. Inability to contract the right orbicularis oculi muscle (6%)
C. Loss of sensation from anterior two-thirds of the tongue (4%)
D. Vision defect affecting the left half of the visual field (10%)
✓ E. Weakness of the right lateral rectus muscle (75%)

Correct

75%
Answered correctly

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Last Updated



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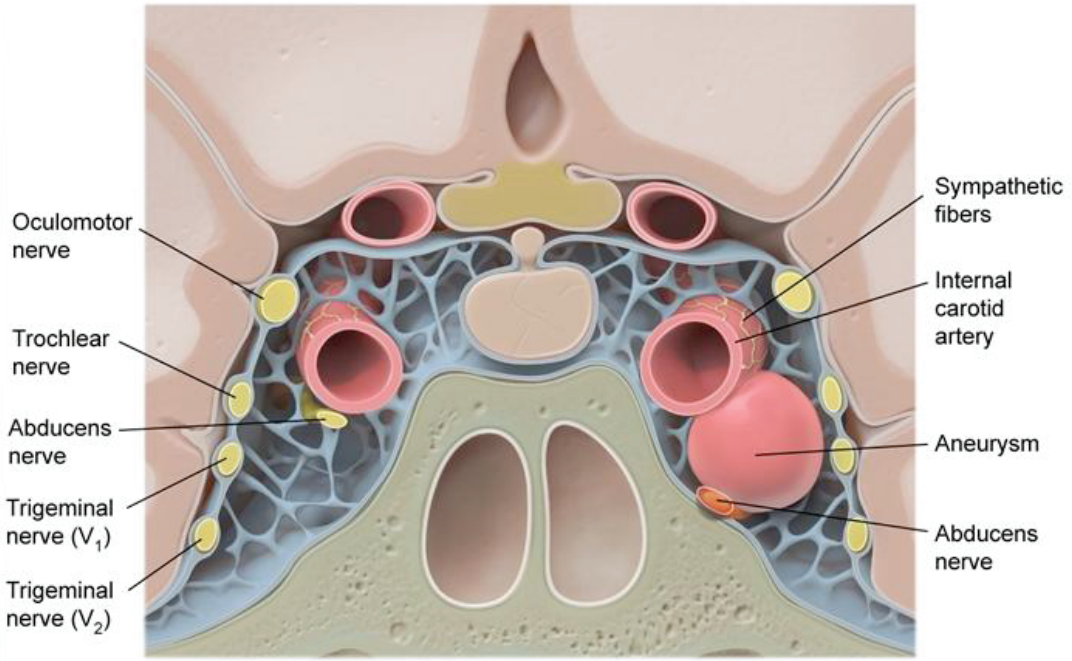
## Cavernous carotid aneurysm

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This patient has a **cavernous carotid aneurysm**, which was discovered during an evaluation for a change



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This patient has a **cavernous carotid aneurysm**, which was discovered during an evaluation for a change in headache frequency and severity from past migraines. Small aneurysms of the cavernous segment of the internal carotid artery are typically asymptomatic; however, as they enlarge, they can compress nearby structures and cause a unilateral, throbbing headache and/or cranial nerve deficits.

The **abducens nerve** (CN VI), which passes through the cavernous sinus next to the internal carotid artery, is the most likely structure to be damaged by an expanding aneurysm. Compression or stretching of the nerve results in **ipsilateral lateral rectus weakness**, which can cause esotropia (**inward eye deviation**) and horizontal **diplopia** (double vision) that is worse when looking toward the side of the lesion.

Other nerves that can be damaged by a cavernous carotid aneurysm include the oculomotor nerve (CN III), trochlear nerve (CN IV), and V1 and V2 branches of the trigeminal nerve (CN V), all of which run on the lateral wall of the cavernous sinus.

**(Choice A)** The hypoglossal nerves (CN XII) innervate the genioglossus muscles, which are responsible for tongue protrusion. Injury to the right hypoglossal nerve (most commonly during carotid endarterectomy) would cause ipsilateral genioglossus weakness with deviation of the tongue to the right during protrusion.

**(Choice B)** Muscles of facial expression, including the orbicularis oculi, are innervated by the facial nerve (CN VII). Damage to the lower motor neurons of the facial nerve (eg, parotid gland tumor, trauma) often


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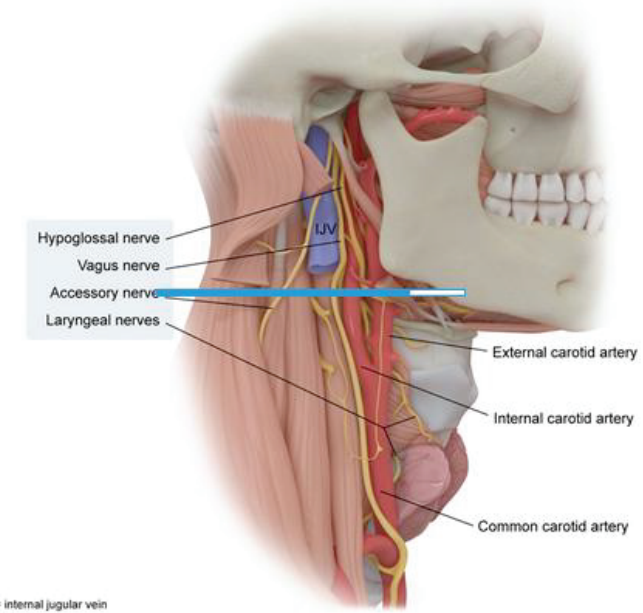
This patient has a **cavernous carotid aneurysm**, which was discovered during an evaluation for a change

Exhibit Display

Nerve at risk during carotid endarterectomy

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This patient has a **cavernous carotid aneurysm**, which was discovered during an evaluation for a change

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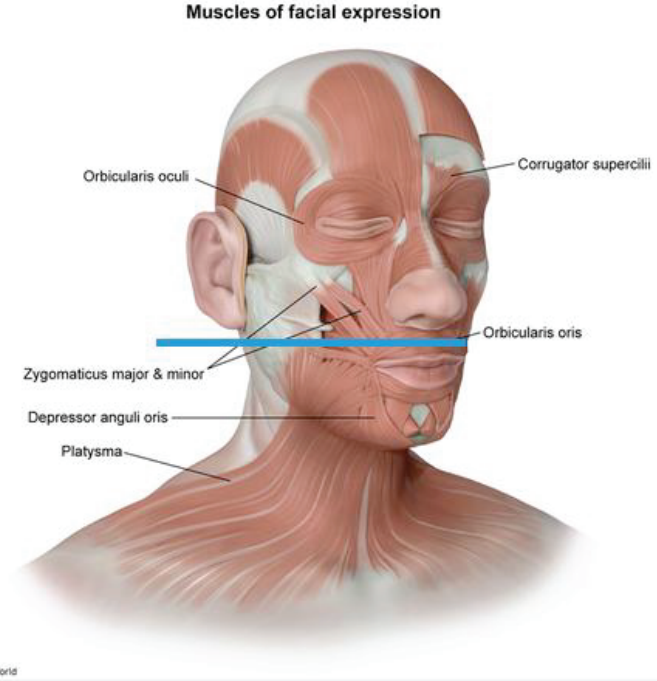


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(CN VII). Damage to the lower motor neurons of the facial nerve (eg, parotid gland tumor, trauma) often results in complete paralysis of ipsilateral facial muscles.

**(Choice C)** General sensation from the anterior two-thirds of the tongue is carried by the lingual nerve (mandibular division of the trigeminal nerve), which, unlike the other 2 divisions of the trigeminal nerve, does not course through the cavernous sinus.

**(Choice D)** Homonymous hemianopia is a defect in half of the visual field due to a contralateral lesion in the visual pathways posterior to the optic chiasm (eg, optic tract, optic radiations). Cavernous carotid aneurysms can occasionally compress the optic nerve or chiasm, usually resulting in ipsilateral monocular vision loss or a nonspecific decrease in visual acuity rather than homonymous hemianopia.

**Educational objective:**
An expanding aneurysm in the cavernous portion of the internal carotid artery (ICA) is most likely to initially cause headache and diplopia (ipsilateral lateral rectus weakness) due to compressing or stretching of the abducens nerve (CN VI) as it runs next to the ICA in the cavernous sinus. Other commonly affected nerves include the oculomotor nerve (CN III), trochlear nerve (CN IV), and the V1 and V2 branches of the trigeminal nerve (CN V).

Anatomy Nervous System Abducens palsy



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A 72-year-old man with a history of Parkinson disease comes to the office for follow-up. The patient has been taking levodopa/carbidopa since being diagnosed 5 years ago, and has required increasing doses of medication to control his symptoms. He is currently on a maximum dose, but for the past several months has experienced bothersome motor fluctuations. The patient also reports worsening stiffness and difficulty moving before his next scheduled dose, which improves after taking the medication. Entacapone is added to his treatment regimen. This drug most likely improves this patient's symptoms by which of the following mechanisms?

A. Decreasing peripheral levodopa degradation
B. Directly stimulating dopamine receptors
C. Enhancing the effect of endogenous dopamine
D. Inhibiting central muscarinic receptors
E. Inhibiting centrally-active acetylcholinesterase

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A 72-year-old man with a history of Parkinson disease comes to the office for follow-up. The patient has been taking levodopa/carbidopa since being diagnosed 5 years ago, and has required increasing doses of medication to control his symptoms. He is currently on a maximum dose, but for the past several months has experienced bothersome motor fluctuations. The patient also reports worsening stiffness and difficulty moving before his next scheduled dose, which improves after taking the medication. Entacapone is added to his treatment regimen. This drug most likely improves this patient's symptoms by which of the following mechanisms?

- A. Decreasing peripheral levodopa degradation (61%)
- B. Directly stimulating dopamine receptors (9%)
- C. Enhancing the effect of endogenous dopamine (18%)
- D. Inhibiting central muscarinic receptors (5%)
- E. Inhibiting centrally-active acetylcholinesterase (5%)


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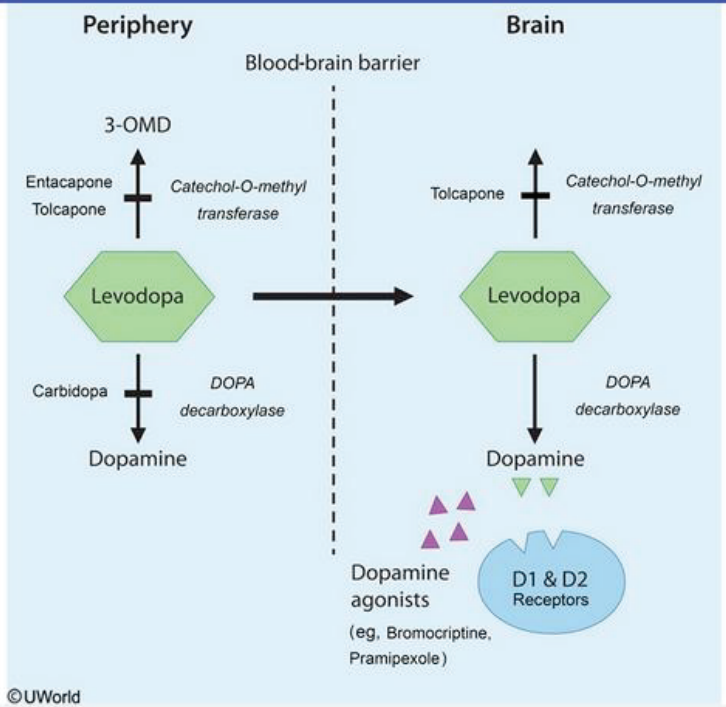


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**Levodopa** is the immediate precursor of dopamine, a neurotransmitter that is absent in the nigrostriatum of patients with **Parkinson disease**. Dopamine itself cannot be administered directly due to its inability to cross the blood-brain barrier; however, levodopa can cross this barrier. Levodopa is rapidly metabolized in the peripheral tissues to dopamine (via DOPA decarboxylase) and 3-O-methyldopa (via catechol-O-methyltransferase [COMT]). Therefore, only a small percentage of levodopa reaches the brain. Consequently, levodopa is typically administered with carbidopa, a peripheral DOPA decarboxylase inhibitor, but even then only 5%-10% of levodopa reaches the brain.

**Entacapone** is a **COMT inhibitor** that increases the bioavailability of levodopa by inhibiting its **peripheral** methylation. Combining levodopa with entacapone helps increase the plasma half-life of levodopa, producing more stable levodopa plasma concentrations and prolonging the therapeutic effect of each dose. COMT inhibitors are currently used to treat Parkinson disease patients with motor fluctuations who are experiencing end-of-dose "wearing off" periods with levodopa/carbidopa therapy. COMT inhibitors should only be used in combination with levodopa, as they are otherwise ineffective.

**(Choice B)** Dopamine agonists (eg, bromocriptine, pramipexole, ropinirole) preferentially stimulate dopamine 2 receptors.

**(Choice C)** Amantadine likely enhances the effect of endogenous dopamine by increasing dopamine


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dopamine 2 receptors.

**(Choice C)** Amantadine likely enhances the effect of endogenous dopamine by increasing dopamine synthesis/release and inhibiting the reuptake of dopamine.

**(Choice D)** Anticholinergics such as trihexyphenidyl and benztropine inhibit central muscarinic receptors. These drugs are mainly used for drug-induced parkinsonism, but patients with tremor as the predominant symptom also respond well.

**(Choice E)** Acetylcholinesterase inhibitors (eg, donepezil, rivastigmine) increase the amount of acetylcholine in the central nervous system. These drugs are commonly used in patients with dementia to increase cholinergic activity in the prefrontal cortex. However, they should be used cautiously in patients with Parkinson disease as higher levels of acetylcholine in the basal ganglia can exacerbate symptoms.

**Educational objective:**
Parkinson disease is typically treated with levodopa (immediate precursor of dopamine), which crosses the blood-brain barrier. Levodopa is administered with DOPA decarboxylase inhibitors (eg, carbidopa) and sometimes catechol-O-methyltransferase inhibitors (eg, entacapone) to reduce the peripheral metabolism of levodopa, resulting in increased levodopa bioavailability to the brain.


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A 55-year-old man comes to the clinic due to headache and progressive facial weakness. The patient's headaches began 2 months ago and are characterized as throbbing. They are typically worse in the morning and when he bears down or coughs. He has had no recent head trauma or loss of consciousness. The patient has a history of hypertension for which he takes lisinopril. He does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. On physical examination, there is flattening of the left nasolabial fold and drooping of the left lower lip. The patient cannot fully close his left eye. MRI of the brain reveals a well-circumscribed homogenously enhancing mass in the posterior fossa that is compressing the left facial nerve root. Which of the following additional findings is most likely present on this patient's neurologic examination?

A. "Down and out" eye deviation
B. Hoarseness of voice
C. Increased sensitivity to sound
D. Loss of facial sensation
E. Loss of hearing



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A. "Down and out" eye deviation
B. Hoarseness of voice
C. Increased sensitivity to sound
D. Loss of facial sensation
E. Loss of hearing
F. Loss of taste in posterior tongue
G. Sensory loss in posterior tongue
H. Tongue deviation to the left



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left nasolabial fold and drooping of the left lower lip. The patient cannot fully close his left eye. MRI of the brain reveals a well-circumscribed homogenously enhancing mass in the posterior fossa that is compressing the left facial nerve root. Which of the following additional findings is most likely present on this patient's neurologic examination?

A. "Down and out" eye deviation (1%)
B. Hoarseness of voice (0%)
C. Increased sensitivity to sound (70%)
D. ~~Loss of facial sensation~~ (5%)
E. Loss of hearing (14%)
F. ~~Loss of taste in posterior tongue~~ (3%)
G. ~~Sensory loss in posterior tongue~~ (1%)
H. ~~Tongue deviation to the left~~ (1%)

70%
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This patient has **facial nerve (CN VII) palsy**, likely due to nerve compression by a meningioma (eg, well-circumscribed, homogenously enhancing mass) in the posterior fossa. Space-occupying intracranial lesions classically present with a headache that is worse in the morning and with Valsalva (eg, bearing down, coughing) due to increased intracranial pressure.

The facial nerve exits the brainstem at the pontomedullary junction and subsequently enters the internal auditory meatus and facial canal in the temporal bone. Here, it gives off branches that supply the stapedius muscle (reduces volume by dampening ossicle movement in middle ear), salivary glands (eg, sublingual, submandibular), and lacrimal glands. It also provides taste from the anterior two thirds of the tongue via the chorda tympani nerve. After exiting the skull through the stylomastoid foramen, the facial nerve courses within the parotid gland and its terminal branches innervate the muscles of facial expression.

Facial nerve palsy presents with ipsilateral facial paralysis (eg, flattening of the nasolabial fold, drooping of the lower lip, inability to close the eye). There is also **loss of the corneal reflex** (efferent limb) due to denervation of the orbicularis oculi muscle. Paralysis of the stapedius muscle may lead to increased sensitivity to sound (**hyperacusis**). Since the nerve to the stapedius is one of the first branches of the facial nerve, hyperacusis indicates that the facial nerve is injured **near its brainstem origin**. Other features of facial nerve palsy include decreased lacrimation, salivation, and **loss of taste** in the **anterior**


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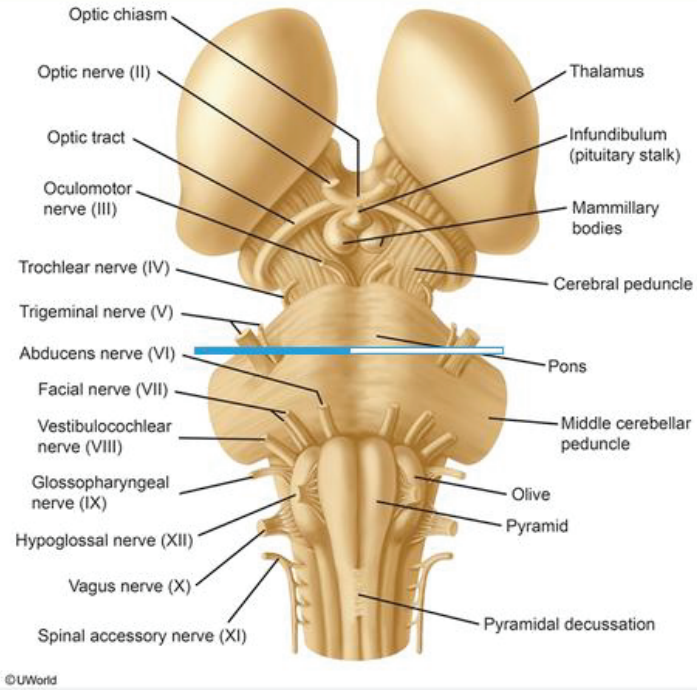


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features of facial nerve palsy include decreased lacrimation, salivation, and **loss of taste** in the **anterior**



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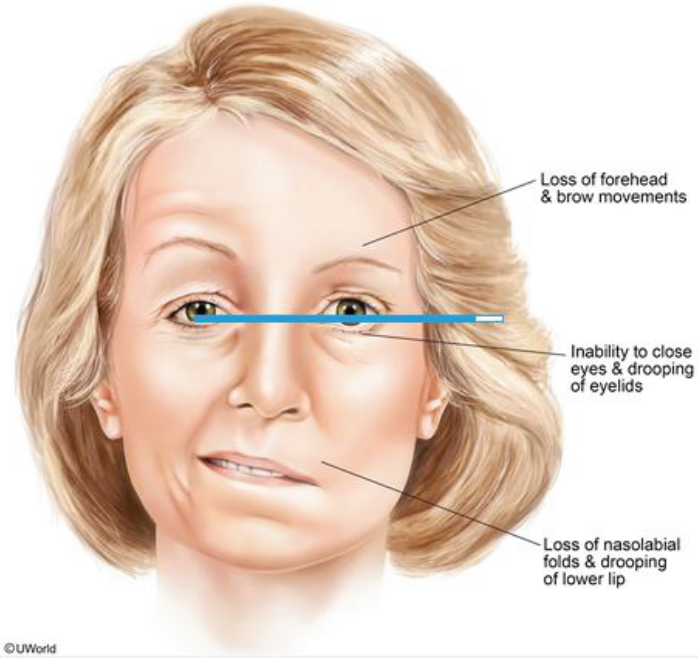
Peripheral facial palsy

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sensitivity to sound (**hyperacusis**). Since the nerve to the stapedius is one of the first branches of the facial nerve, hyperacusis indicates that the facial nerve is injured **near its brainstem origin**. Other features of facial nerve palsy include decreased lacrimation, salivation, and **loss of taste** in the **anterior two thirds** of the tongue.

**(Choice A)** Oculomotor nerve (CN III) palsy causes "down and out" eye deviation, ptosis (due to levator palpebrae superioris paralysis), and a fixed dilated pupil (due to parasympathetic fiber injury).

**(Choice B)** Vagus nerve (CN X) injury causes paralysis of the soft palate (eg, loss of efferent limb of the gag reflex), pharyngeal muscles (eg, dysphagia), and laryngeal muscles (eg, hoarseness). Sensory loss in the larynx and pharynx may also lead to impaired cough reflex.

**(Choice D)** Trigeminal nerve (CN V) damage causes ipsilateral facial anesthesia, loss of the corneal reflex (afferent limb), weakness of the muscles of mastication, and jaw deviation toward the side of the lesion (due to unopposed action of the opposite pterygoid muscle).

**(Choice E)** Vestibulocochlear nerve (CN VIII) injury (eg, due to vestibular schwannoma) causes sensorineural hearing loss, tinnitus, and vertigo.

**(Choices F and G)** Glossopharyngeal nerve (CN IX) damage causes loss of sensation and taste in the posterior one third of the tongue, and loss of the gag reflex (afferent limb).



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**(Choice E)** Vestibulocochlear nerve (CN VIII) injury (eg, due to vestibular schwannoma) causes sensorineural hearing loss, tinnitus, and vertigo.

**(Choices F and G)** Glossopharyngeal nerve (CN IX) damage causes loss of sensation and taste in the posterior one third of the tongue, and loss of the gag reflex (afferent limb).

**(Choice H)** Hypoglossal nerve (CN XII) injury causes tongue weakness and deviation toward the side of the lesion.

**Educational objective:**
Hyperacusis (increased sensitivity to sound) is an indication of damage to the facial nerve (CN VII) close to its origin from the brainstem.

**References**

- Hyperacusis.
- Seventh cranial neuropathy.



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A 23-year-old man is evaluated for prolonged paralysis following general anesthesia for an elective surgical procedure. Anesthesia was induced with propofol, succinylcholine was used for intubation, and anesthesia was maintained via propofol and fentanyl infusions. The patient has not had a return of neuromuscular function after several hours. His mother then discloses that she has also been "slow to wake up" from anesthesia. Which of the following is the most likely reason for this patient's prolonged paralysis?

A. Decreased first-pass metabolism
B. Decreased plasma hydrolysis
C. Increased binding to plasma proteins
D. Increased redistribution to fat
E. Upregulation of target receptors

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A. Decreased first-pass metabolism (21%)
B. Decreased plasma hydrolysis (39%)
C. Increased binding to plasma proteins (8%)
D. Increased redistribution to fat (14%)
E. Upregulation of target receptors (15%)

Correct

39%
Answered correctly

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Time Spent

10/08/2020
Last Updated



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This patient who developed prolonged muscle weakness (eg, failure of spontaneous respiration, voluntary muscle activity) after receiving succinylcholine most likely has pseudocholinesterase deficiency, an autosomal recessive disorder caused by a genetic polymorphism in the *BCHE* gene.

**Succinylcholine** is a depolarizing neuromuscular blocking agent used to induce skeletal muscle relaxation during intubation and surgery. It acts as a **competitive agonist** of **nicotinic acetylcholine receptors** of the motor endplate, where it induces **persistent depolarization**, leading to desensitization and skeletal muscle paralysis. Succinylcholine is rapidly **hydrolyzed by plasma pseudocholinesterase**; only around 10% of the administered dose reaches the neuromuscular junction, where it typically has a duration of action of <10 minutes.

Patients with **pseudocholinesterase deficiency** are unable to metabolize succinylcholine, which leads to a large amount of the drug reaching the neuromuscular junction. Heterozygotes may experience double the normal duration of paralysis; homozygotes can have persistent **paralysis for several hours**.

**(Choice A)** Decreased first-pass metabolism often occurs when drugs are administered via a nonoral route, allowing them to reach the systemic circulation without passing through the portal circulation and liver. Although succinylcholine is given intravenously, it is primarily inactivated in the plasma by


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liver. Although succinylcholine is given intravenously, it is primarily inactivated in the plasma by pseudocholinesterase rather than the liver.

**(Choice C)** The pharmacologic effects of drugs are typically enacted by the unbound (free) form of the drug. Therefore, increased binding to plasma proteins would likely decrease (rather than increase) the effect of the medication.

**(Choice D)** Propofol is highly lipid soluble and has a very short duration of action (seconds) because of rapid redistribution from the brain (where it activates the GABA-A receptor) to other tissues (predominantly fat). However, propofol is a hypnotic agent; it does not cause muscle paralysis.

**(Choice E)** Upregulation of target receptors would increase sensitivity to acetylcholine, which is one possible mechanism of spasticity in cerebral palsy. However, receptor upregulation occurs over many hours or days, not with a first dose.

**Educational objective:**
Succinylcholine, a depolarizing neuromuscular blocking agent, is rapidly hydrolyzed by plasma pseudocholinesterase. Patients with pseudocholinesterase deficiency have prolonged neuromuscular paralysis after drug administration.

Pharmacology Nervous System Anesthesia



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A 49-year-old woman comes to the office due to muscle weakness. For the past 3 months, the patient has had worsening weakness in her right hand. She has also been tripping. The patient experiences twitching and cramping in her arms and legs. She has no sensory deficits. On examination, there is increased tone and fasciculations in the lower extremity muscles. Atrophy of the interosseus muscles of the right hand and the bilateral intrinsic muscles of the feet is present. When the physician taps on the chin while the mouth is slightly open, the jaw jerks upward briskly. Which of the following cranial nerves mediate this reflex?

| | Afferent | Efferent |
|---|---|---|
| A. | Glossopharyngeal | Trigeminal |
| B. | Glossopharyngeal | Vagus |
| C. | Trigeminal | Facial |
| D. | Trigeminal | Trigeminal |
| E. | Vagus | Vagus |

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| | Afferent | Efferent | |
|---|---|---|---|
| A. | Glossopharyngeal | Trigeminal | (2%) |
| B. | Glossopharyngeal | Vagus | (1%) |
| C. | Trigeminal | Facial | (30%) |
| ✓ D. | Trigeminal | Trigeminal | (64%) |
| E. | Vagus | Vagus | (0%) |



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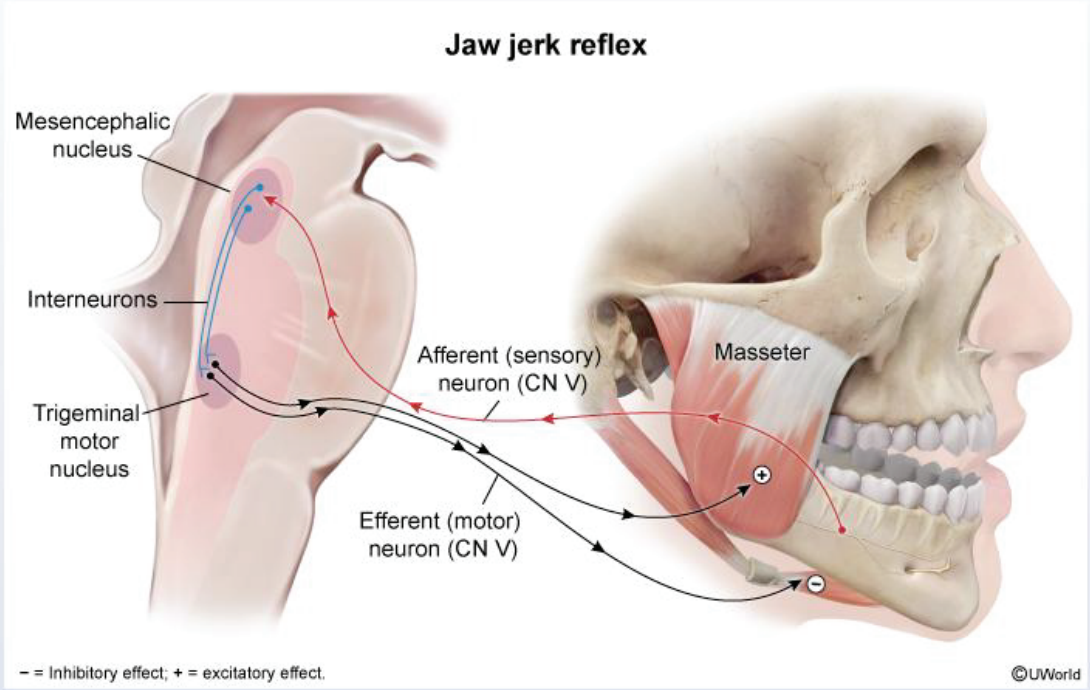
Explanation




This patient with findings of both upper (spasticity, increased tone) and lower (atrophy, fasciculations) motor



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− = Inhibitory effect; + = excitatory effect.

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This patient with findings of both upper (spasticity, increased tone) and lower (atrophy, fasciculations) motor neuron lesions most likely has amyotrophic lateral sclerosis (ALS). Tapping on the chin with the mouth slightly open causes the jaw to briskly close, which represents a positive (ie, pathologic) **jaw jerk reflex**. This reflex is **normally absent** or very weak but is present in patients with bilateral upper motor neuron lesions such as ALS.

The jaw jerk reflex begins with **afferent** signals from muscle spindles of the masseter that are carried along the mandibular division of the **trigeminal nerve** (CN V3) to the trigeminal mesencephalic nucleus, which is involved with reflex proprioception of the muscles of mastication. This center then coordinates with the trigeminal motor nucleus to send motor **(efferent)** signals back along CN V3 to the muscles of mastication, causing the jaw to close.

The jaw jerk reflex is the only tendon reflex mediated above the plane of the foramen magnum. Therefore, the pathologic presence of this reflex suggests **bilateral lesions of the upper motor neuron** pathways **above** the level of the **pons** (eg, ALS, multiple sclerosis, pseudobulbar palsy).

**(Choices A and B)** Sensory fibers of the glossopharyngeal nerve (CN IX) are involved in both the gag and the carotid sinus reflexes. The gag reflex is mediated via afferent information from the glossopharyngeal



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**above** the level of the **pons** (eg, ALS, multiple sclerosis, pseudobulbar palsy).

**(Choices A and B)** Sensory fibers of the glossopharyngeal nerve (CN IX) are involved in both the gag and the carotid sinus reflexes. The gag reflex is mediated via afferent information from the glossopharyngeal nerve (CN IX), and efferent information from the vagus nerve (CN X). The carotid sinus reflex is mediated by afferent signals from arterial baroreceptors which are carried to the brainstem by CN IX and CN X; efferent signals are then carried by parasympathetic fibers to the sinoatrial and atrioventricular nodes.

**(Choice C)** The corneal reflex is mediated by afferent fibers from the ophthalmic division of the trigeminal nerve (CN V1) and efferent fibers of the facial nerve (CN VII) projecting to the orbicularis oculi muscle, causing a blink.

**(Choice E)** Both the afferent and the efferent limbs of the cough reflex are mediated by the vagus nerve (CN X).

**Educational objective:**
The jaw jerk reflex is a pathologic cranial nerve reflex present in patients with bilateral upper motor neuron lesions, such as amyotrophic lateral sclerosis. Both the afferent and efferent pathways are mediated by the mandibular division of the trigeminal nerve (CN V3).


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**(Choices A and B)** the carotid sinus re nerve (CN IX), and by afferent signals efferent signals are

**(Choice C)** The co nerve (CN V1) and causing a blink.

**(Choice E)** Both th (CN X).

**Educational objec**
The jaw jerk reflex lesions, such as an mandibular division

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**Cranial nerve reflexes**

| Reflex | Effect | Afferent | Efferent |
|---|---|---|---|
| **Pupillary light reflex** | Light-induced pupil constriction | II | III |
| **Corneal reflex** | Corneal stimulation causing orbicularis oculi to contract eyelids | V1 (ophthalmic branch) | VII |
| **Jaw jerk reflex*** | Stretch reflex stimulating masseter contraction | V3 (sensory from muscle spindles) | V3 |
| **Vestibuloocular reflex** | Compensatory eye movements that provide image stabilization when head/body moves | VIII (vestibular component) | III, IV, VI |
| **Carotid sinus reflex** | Increased carotid sinus pressure that causes decreased heart rate & blood pressure | IX | X (sympathetic tone also inhibited) |
| **Cough reflex** | Cough induced by upper respiratory tract irritation | X | X |
| | Reflex contraction of pharyngeal | | |

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| | | | |
|---|---|---|---|
| **reflex** | Light-induced pupil constriction | II | III |
| **Corneal reflex** | Corneal stimulation causing orbicularis oculi to contract eyelids | V1 (ophthalmic branch) | VII |
| **Jaw jerk reflex*** | Stretch reflex stimulating masseter contraction | V3 (sensory from muscle spindles) | V3 |
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| **Carotid sinus reflex** | Increased carotid sinus pressure that causes decreased heart rate & blood pressure | IX | X (sympathetic tone also inhibited) |
| **Cough reflex** | Cough induced by upper respiratory tract irritation | X | X |
| **Gag reflex** | Reflex contraction of pharyngeal constrictor muscles evoked by touching back of throat | IX | X |

*Pathologic reflex present in patients with bilateral upper motor neuron lesions (eg, amyotrophic lateral sclerosis).

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trigeminal motor nucleus to send motor **(efferent)** signals back along CN V3 to the muscles of mastication;

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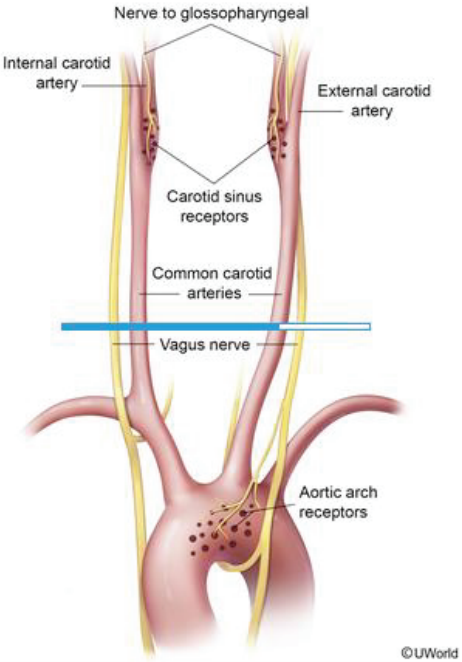
**Carotid sinus & aortic arch baroreceptors**

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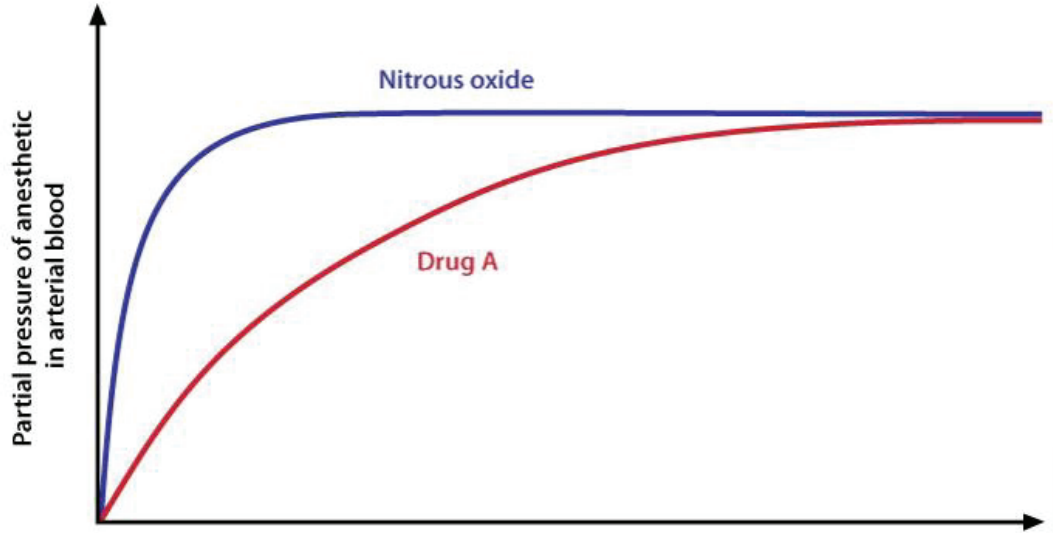
A new inhaled agent (drug A) is tested in an experiment designed to characterize its properties as a general anesthetic. Drug A's partial pressure in arterial blood is shown on the graph below as a function of time after beginning inhalation. A similar curve for nitrous oxide is also shown. Both drugs are administered at the same partial pressure in the inspired gas.

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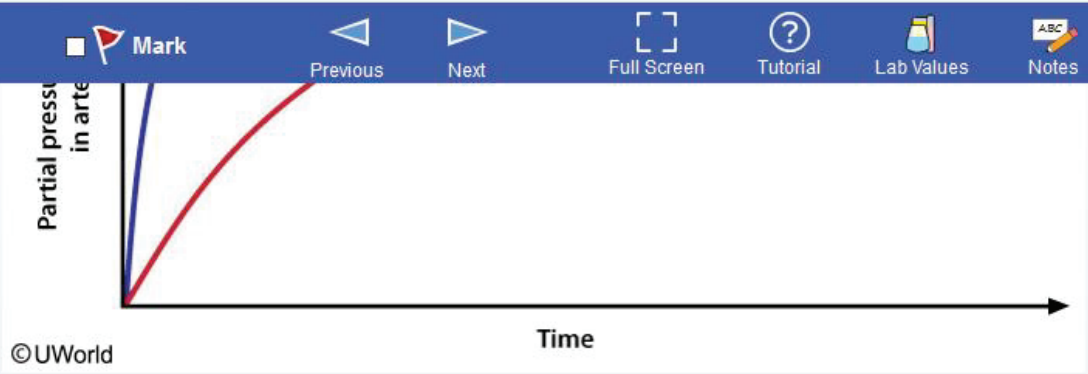


Which of the following best describes the properties of the new anesthetic as compared to nitrous oxide?

A. Fast equilibration with the brain
B. High blood/gas partitioning coefficient
C. Low potency
D. Low solubility in the blood
E. Rapid onset of action

Submit



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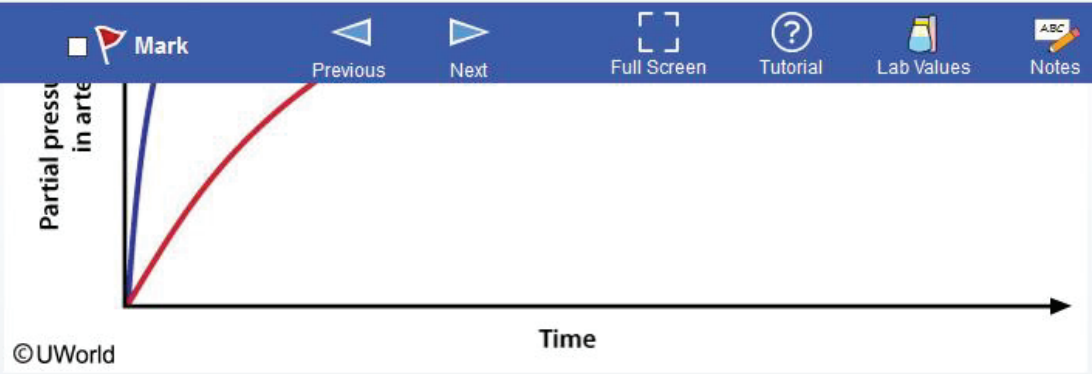


Which of the following best describes the properties of the new anesthetic as compared to nitrous oxide?

A. ~~Fast equilibration with the brain~~ (4%)

✓ B. High blood/gas partitioning coefficient (37%)

✗ C. Low potency (17%)

D. ~~Low solubility in the blood~~ (33%)

E. ~~Rapid onset of action~~ (7%)

Incorrect
Correct answer

37%

03 mins

01/11/2021



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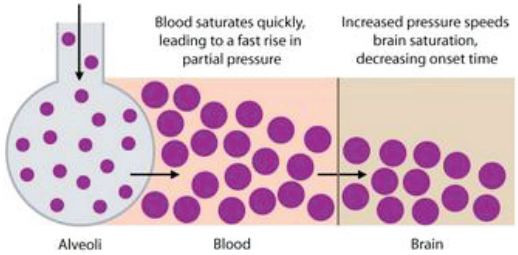
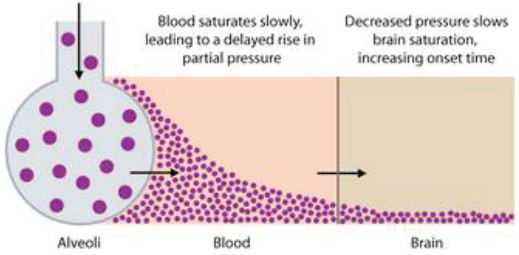
## Exhibit Display

**Effects of solubility on the onset of gas anesthetics**

Poorly soluble gas (↓blood/ gas partition coefficient)




Highly soluble gas (↑blood/ gas partition coefficient)

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During anesthetic induction with a gaseous agent, the partial pressure of the anesthetic rises in the blood until it reaches its partial pressure in the inspired gas. At this point, no more of the anesthetic can dissolve in the blood and the blood is said to be saturated with the anesthetic. The speed at which the blood becomes saturated depends on the solubility of the gas in the blood. Highly soluble anesthetics dissolve easily in the blood, and thus larger amounts must be absorbed before the blood becomes saturated.

Blood solubility of an anesthetic is indicated by its **blood/gas partition coefficient** - anesthetics with higher blood solubility have larger blood/gas partition coefficients. Nitrous oxide ($N_2O$) is an example of a poorly soluble gas with a blood/gas partition coefficient of 0.47. In the graph above, the partial pressure of $N_2O$ in blood rises rapidly and plateaus, indicating that the blood quickly becomes saturated with the anesthetic. In contrast, drug A has higher solubility (ie, a larger blood/gas partition coefficient) as its partial pressure in the blood rises more slowly. The curve for drug A eventually levels out at the same partial pressure as $N_2O$ since the drugs are inspired at equal partial pressures. However, by this point, far more drug A is dissolved in the blood.

The speed of anesthetic induction is determined by the rate at which the brain tissues take up the agent, which is dependent on the solubility of the anesthetic in the blood. If an agent has poor blood solubility, the amount of gas needed to saturate the blood is small and brain saturation occurs fairly quickly. Conversely



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The speed of anesthetic induction is determined by the rate at which the brain tissues take up the agent, which is dependent on the solubility of the anesthetic in the blood. If an agent has poor blood solubility, the amount of gas needed to saturate the blood is small and brain saturation occurs fairly quickly. Conversely, highly soluble anesthetics are absorbed to a greater degree by the blood, delaying saturation of the central nervous system.

**Characteristics of gas anesthetics**

| Effect | Poorly soluble gas ($N_2O$) | Highly soluble gas (halothane) |
|---|---|---|
| Amount needed to saturate the blood | Small | Large |
| Rise in partial pressure in blood | Rapid | Slow |
| Equilibration with the brain | Rapid | Slow |
| Onset of action | Rapid | Slow |

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| | | |
|---|---|---|
| Onset of action | Rapid | Slow |

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**(Choices A, D, and E)** Nitrous oxide is an example of a gas with relatively low solubility in the blood. It is characterized by rapid onset of action and fast equilibration with the brain.

**(Choice C)** Potency of a gas anesthetic is determined by the minimal alveolar concentration. It is defined as the concentration of gas in the lungs that produces the desired effect in 50% of patients. Potent anesthetics require lower partial pressures to be effective.

**Educational objective:**

The onset of action of a gas anesthetic depends on its solubility in the blood (blood/gas partition coefficient). Drugs with high blood/gas partition coefficients are more soluble in the blood, demonstrate slower equilibration with the brain, and have longer onset times.

| Pharmacology | Nervous System | Drug structure and properties |
|---|---|---|
| Subject | System | Topic |

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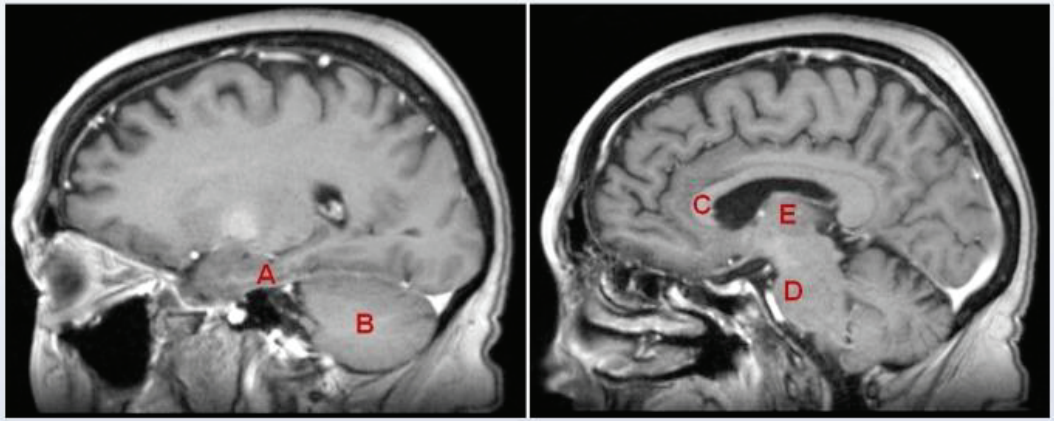
A 71-year-old woman is brought to the physician by her daughter. She says that her mother went shopping yesterday and could not find her way back home. Two years ago, her mother "started forgetting things like where she put her keys" and "began to have problems remembering the right words." Now she has trouble keeping up with her activities of daily living and refuses to pay her bills because "it's a waste of money." The patient's past medical history is unremarkable. Brain magnetic resonance imaging (MRI) is most likely to show atrophy of which of the following structures?




A. A



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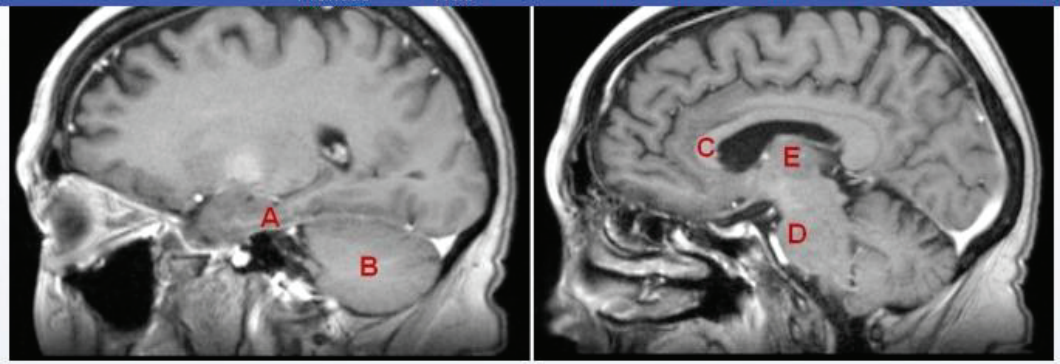


A.A

B.B

C.C

D.D

E.E

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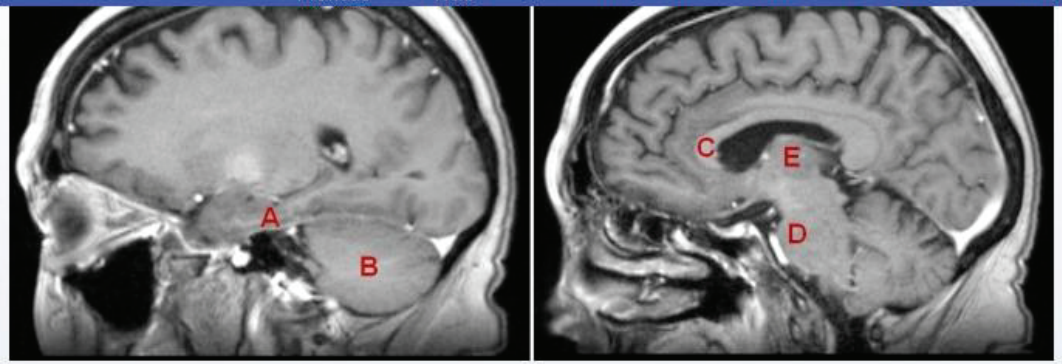


- ✓ A.A (57%)
- B.B (1%)
- C.C (19%)
- D.D (3%)
- ✗ E.E (17%)

Incorrect
Correct answer

57%

46 secs

02/08/2021



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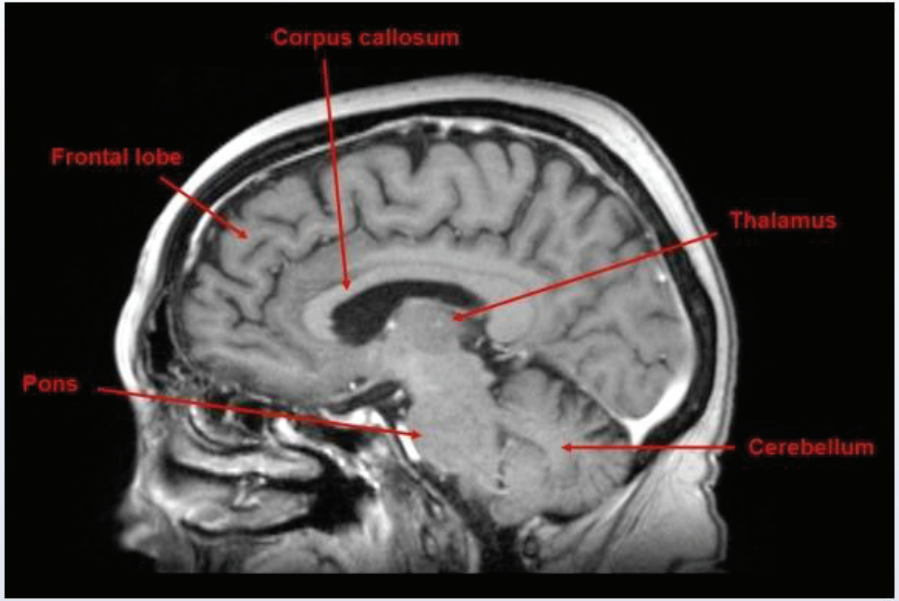
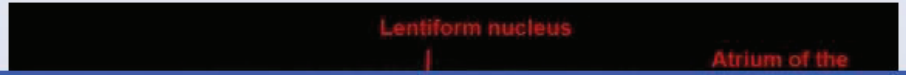
## Explanation



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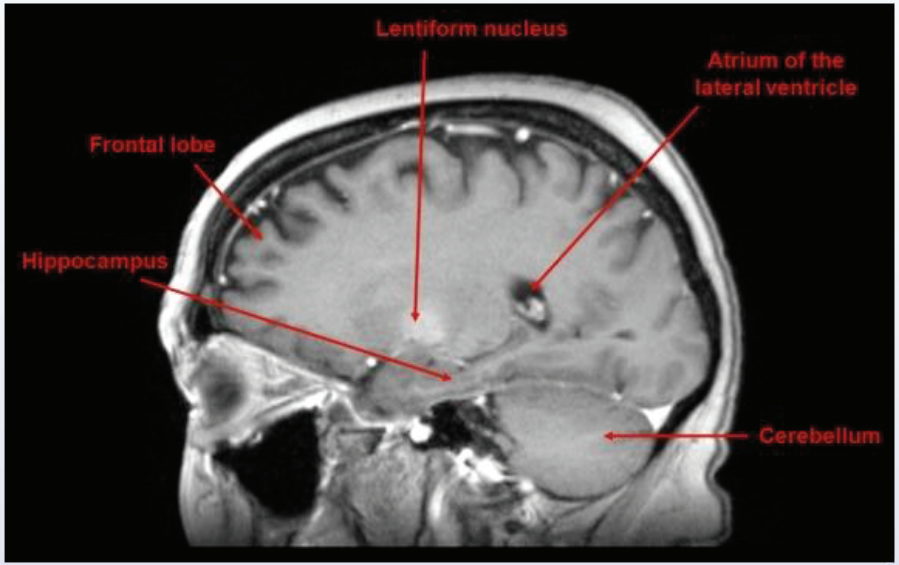


Alzheimer's disease is a neurodegenerative disorder that presents with insidiously progressive memory loss. It is the most common cause of dementia and usually affects people > 60 years of age. Language


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Alzheimer's disease is a neurodegenerative disorder that presents with insidiously progressive memory loss. It is the most common cause of dementia and usually affects people > 60 years of age. Language deficits (word-finding difficulty) and impaired visuospatial ability (misplacement of items) can occur early in the course of the disease. Later, as impairment in executive function and associated behavioral abnormalities become more pronounced, patients can have trouble performing everyday functions (eg, shopping, cooking, and managing money).

Advanced Alzheimer's disease is associated with diffuse brain atrophy. Atrophy is most pronounced in the temporoparietal lobes and hippocampus. Hippocampal atrophy is evident even in the early stages of the disease and can be detected by brain MRI.

The cerebellum **(Choice B)**, corpus callosum **(Choice C)**, pons **(Choice D)**, and thalamus **(Choice E)** are not obviously atrophied in Alzheimer's disease.

**Educational objective:**
The hippocampus is the area of the brain demonstrating the greatest degree of atrophy in Alzheimer's disease. Hippocampal atrophy on MRI is highly suggestive of the diagnosis.

Pathology Nervous System Alzheimer disease



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A 71-year-old man comes to the office due to a painful rash on his right forehead. Two days ago, he felt burning pain on his right forehead and today noticed some blisters. On examination, there is a vesicular rash involving the right forehead and right side of the nose. The patient is at risk of blindness in the right eye due to involvement of which of the following cranial nerves?

A. Abducens
B. Facial
C. Oculomotor
D. Optic
E. Trigeminal
F. Trochlear

Submit



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A 71-year-old man comes to the office due to a painful rash on his right forehead. Two days ago, he felt burning pain on his right forehead and today noticed some blisters. On examination, there is a vesicular rash involving the right forehead and right side of the nose. The patient is at risk of blindness in the right eye due to involvement of which of the following cranial nerves?

A. ~~Abducens~~ (0%)
B. ~~Facial~~ (2%)
C. ~~Oculomotor~~ (1%)
D. Optic (30%)
E. Trigeminal (64%)
F. Trochlear (0%)

Incorrect
Correct answer
E

64%
Answered correctly

42 secs
Time Spent

03/06/2021
Last Updated



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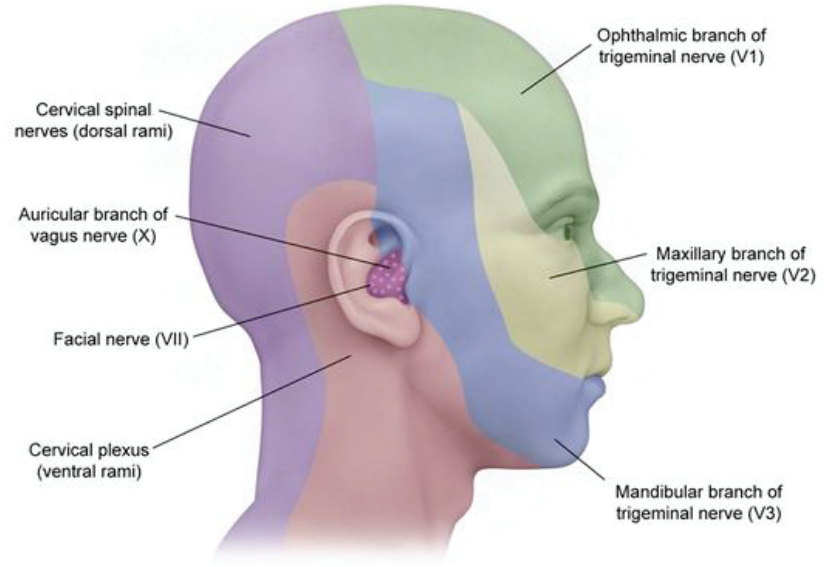
Exhibit Display

Dermatomes of head & neck

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Mandibular branch of



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This patient has **herpes zoster ophthalmicus**, which is caused by reactivation of latent varicella-zoster virus (VZV) in the trigeminal ganglion. Following primary VZV infection (ie, chickenpox), the virus migrates via sensory nerves to the cranial nerve and dorsal spinal ganglia, where it lies **dormant** for years. Reactivation of the virus typically occurs in a single ganglion and causes a painful, vesicular rash in a **dermatomal distribution**.

Viral **reactivation within the trigeminal ganglion** most often affects the ophthalmic division of the trigeminal nerve (CN V1), leading to development of a vesicular rash within the **V1 distribution** (eg, unilateral forehead, side of the nose, and periorbital area). Because CN V1 also conveys sensory innervation of the cornea (sensory limb of the corneal/blink reflex), involvement can cause **acute keratitis**, which can lead to vision loss. Vesicular lesions on the side and tip of the nose (ie, **Hutchinson sign**) have a high correlation with subsequent eye involvement because the nasociliary branch of CN V1 innervates both the eye and the side/tip of the nose.

**(Choices A, C, and F)** The oculomotor (CN III), trochlear (CN IV), and abducens (CN VI) nerves provide motor innervation to the extraocular muscles. Dysfunction can result in double vision. However, these nerves are not involved in this patient's condition and would not cause blindness if they were.



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nerves are not involved in this patient's condition and would not cause blindness if they were.



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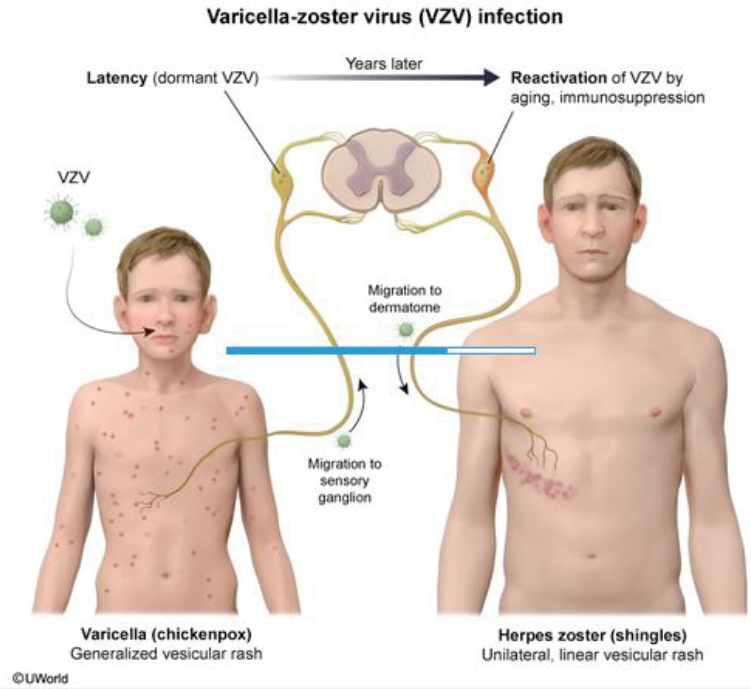


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**(Choices A, C, and F)** The oculomotor (CN III), trochlear (CN IV), and abducens (CN VI) nerves provide motor innervation to the extraocular muscles. Dysfunction can result in double vision. However, these nerves are not involved in this patient's condition and would not cause blindness if they were.

**(Choice B)** The facial nerve (CN VII) is affected in herpes zoster oticus (Ramsay Hunt syndrome), which classically presents with ear pain, vesicles in the external auditory canal or auricle, and facial paralysis. The facial nerve innervates the orbicularis oculi muscle to close the eye; therefore, patients with facial nerve paralysis are at risk of exposure keratitis, which can lead to blindness. However, this patient's facial nerve is unaffected.

**(Choice D)** In rare instances, zoster can cause blindness due to acute retinal necrosis and/or neuritis of the optic nerve (CN II). However, this patient has zoster involvement of CN V1.

**Educational objective:**

Herpes zoster ophthalmicus is caused by viral reactivation within the trigeminal nucleus. It affects the ophthalmic branch of the trigeminal nerve (CN V1) and can lead to blindness due to acute keratitis because V1 conveys sensory information from the cornea.

**References**

- Herpes zoster ophthalmicus: acute keratitis.



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A 62-year-old woman comes to the office for follow-up a month after undergoing left mastectomy and axillary lymph node dissection for invasive ductal carcinoma. Today, the patient feels well overall but reports continued burning and aching in her left upper arm, despite physical therapy. Examination of the left chest wall shows a healing incision without erythema and mild but appropriate edema of the left chest wall and axillary soft tissues. Sensation is diminished in the medial upper arm, near the axilla. Shoulder range of motion is normal, and the rest of the physical examination is unremarkable. Injury to which of the following nerves is most likely responsible for this patient's symptoms?

A. Intercostobrachial
B. Medial pectoral
C. Suprascapular nerve
D. Thoracodorsal

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A 62-year-old woman comes to the office for follow-up a month after undergoing left mastectomy and axillary lymph node dissection for invasive ductal carcinoma. Today, the patient feels well overall but reports continued burning and aching in her left upper arm, despite physical therapy. Examination of the left chest wall shows a healing incision without erythema and mild but appropriate edema of the left chest wall and axillary soft tissues. Sensation is diminished in the medial upper arm, near the axilla. Shoulder range of motion is normal, and the rest of the physical examination is unremarkable. Injury to which of the following nerves is most likely responsible for this patient's symptoms?

- A. Intercostobrachial (43%)
- B. Medial pectoral (22%)
- C. ~~Suprascapular nerve~~ (10%)
- D. ~~Thoracodorsal~~ (23%)

Correct

43%
Answered correctly

01 min, 08 secs
Time Spent

10/14/2020
Last Updated



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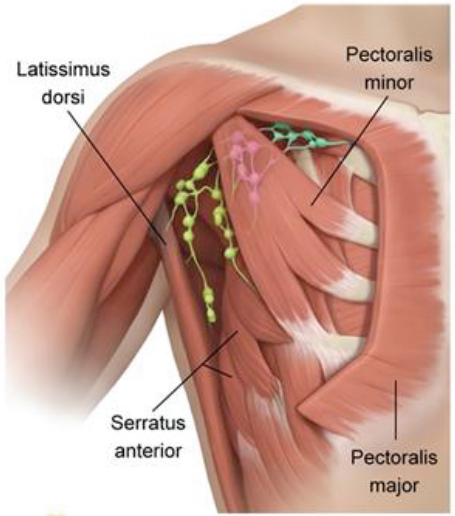
Explanation

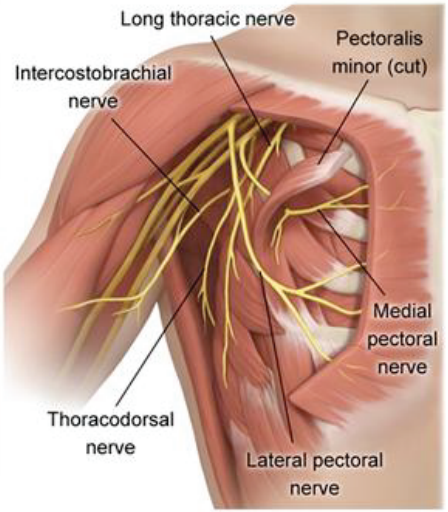
Exhibit Display

Axillary lymph node dissection

Surgical lymph node levels




Nerves at risk

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This patient who underwent **axillary lymph node dissection** has persistent **sensory dysfunction** (eg, burning, aching, diminished sensation) in her **medial upper arm**, findings consistent with **intercostobrachial nerve** injury. The intercostobrachial nerve is a purely sensory nerve that typically originates from the second intercostal nerve's lateral cutaneous branch and then traverses the axilla to innervate the skin of the axilla and medial upper arm.

The intercostobrachial nerve is the most frequently injured nerve (whether by stretching or transection) during axillary lymph node dissection. However, injuries to **other at-risk nerves** are often more feared due to the resultant motor deficits:

- **Long thoracic** nerve (serratus anterior): Damage results in scapular winging and weakness of arm abduction above the horizontal level.
- **Thoracodorsal** nerve (latissimus dorsi): Damage results in loss of powerful adduction of the arm and weakness while extending and medially rotating the arm **(Choice D)**.
- **Medial pectoral** (pectoralis minor and major) and lateral pectoral (pectoralis major) nerves: Damage results in weakness while adducting and medially rotating the arm. In addition, there may be weakness flexing (clavicular head) or extending (sternocostal head) the humerus. **(Choice B)**

This patient has normal shoulder range of motion and an otherwise unremarkable examination (ie, **no**


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This patient has normal shoulder range of motion and an otherwise unremarkable examination (ie, **no motor weakness**), making injury to these nerves less likely. In addition, because the long thoracic, thoracodorsal, and medial and lateral pectoral nerves are primarily motor nerves and not responsible for any cutaneous sensation, their injury would not explain this patient's sensory deficits.

**(Choice C)** The suprascapular nerve provides sensation to the shoulder joint (glenohumeral and acromioclavicular joints) and motor innervation to the supraspinatus and infraspinatus muscles. It branches off the upper trunk of the brachial plexus and travels posteriorly towards the suprascapular notch of the scapula, where it is prone to injury; it does not travel through the axilla and is not at risk during axillary dissection.

**Educational objective:**

Multiple nerves are at risk for injury during axillary lymph node dissection. Intercostobrachial nerve injury results in sensory dysfunction (eg, burning, numbness) to the skin of the axilla and medial upper arm. Injury to the long thoracic (serratus anterior), thoracodorsal (latissimus dorsi), medial pectoral (pectoralis minor and major), or lateral pectoral (pectoralis major) nerves result in motor deficits to corresponding muscles.

**References**



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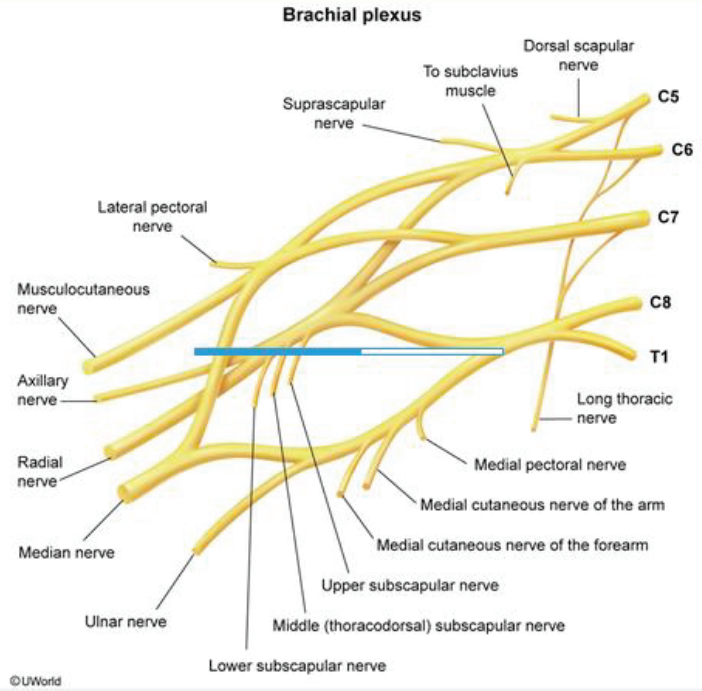


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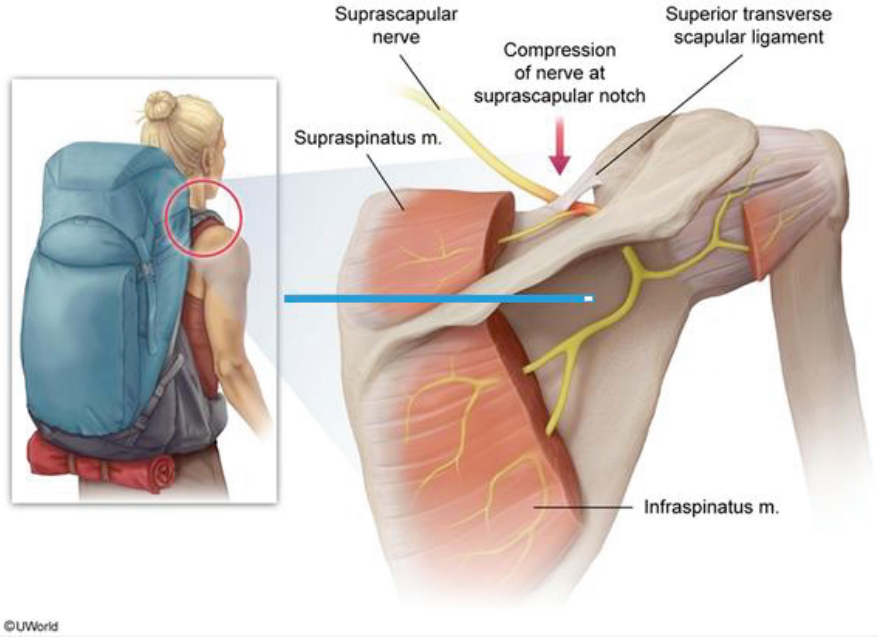
Exhibit Display

## Suprascapular nerve entrapment

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A 16-year-old obese primigravida girl comes to the emergency department in active labor. In an attempt to conceal the pregnancy from her family, the patient did not receive prenatal care or take prenatal vitamins. A fetal heartbeat is undetectable, and she delivers a stillborn boy via vaginal delivery. Examination of the stillborn shows several dysmorphic features including closely set eyes and a midline mass consistent with a proboscis. A fetal autopsy reveals fused cerebral hemispheres with an absent forebrain fissure and a single intracranial ventricle. Which of the following is the most likely mechanism for these findings?

A. Agenesis
B. Association
C. Deformation
D. Dysplasia
E. Field defect

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A 16-year-old obese primigravida girl comes to the emergency department in active labor. In an attempt to conceal the pregnancy from her family, the patient did not receive prenatal care or take prenatal vitamins. A fetal heartbeat is undetectable, and she delivers a stillborn boy via vaginal delivery. Examination of the stillborn shows several dysmorphic features including closely set eyes and a midline mass consistent with a proboscis. A fetal autopsy reveals fused cerebral hemispheres with an absent forebrain fissure and a single intracranial ventricle. Which of the following is the most likely mechanism for these findings?

A. Agenesis (39%)
B. Association (6%)
C. Deformation (27%)
D. Dysplasia (6%)
✓ E. Field defect (19%)

Correct

19%
Answered correctly

01 min, 13 secs
Time Spent

12/30/2020
Last Updated



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| Holoprosencephaly | |
|---|---|
| **Embryology** | • Incomplete forebrain (prosencephalon) division into 2 hemispheres |
| **Etiologies** | • Genetic: Trisomy 13, sonic hedgehog gene mutations<br>• Environmental: maternal alcohol use, retinoic acid |
| **Clinical features** | • CNS abnormalities<br>  ○ Range from asymptomatic to seizures, severe intellectual disability, death<br>• Midface abnormalities<br>  ○ Range from mild hypotelorism and cleft lip/palate to cyclopia, primitive nose, facial cleft |

The physical features of the stillborn are consistent with holoprosencephaly (HPE), which is a spectrum of structural abnormalities of the brain and face due to **incomplete division of the forebrain** (prosencephalon) into 2 hemispheres. Cleavage of the prosencephalon into the telencephalon and diencephalon normally occurs at **5 weeks gestation**. Failure of cleavage at different points in division can result in an array of anomalies ranging from mild midline defects (eg, ocular hypotelorism, cleft lip/palate) to severe defects (eg, single midline eye, primitive nasal structure or proboscis, midfacial clefts).


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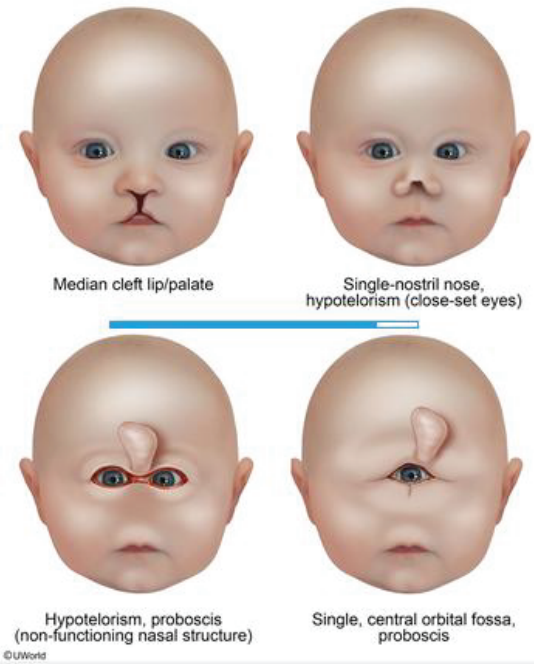
Exhibit Display

Holoprosencephaly spectrum

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severe defects (eg, single midline eye, primitive nasal structure or proboscis, midfacial clefts).

HPE is likely caused by a combination of genetic (eg, trisomy 13, sonic hedgehog gene mutations) and environmental (eg, maternal alcohol use) factors. It is an example of a **developmental field defect**, which is when an initial embryonic disturbance leads to multiple malformations by disrupting the development of adjacent tissues and structures within a particular region.

**(Choice A)** Agenesis refers to the complete absence of an organ. Renal agenesis, the congenital absence of one or both kidneys, is an example of this type of abnormality.

**(Choice B)** An association refers to multiple anomalies without a known unifying cause that occur together more frequently than chance alone would predict. Vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities (VACTERL) are an example of an association of anomalies without a known common etiology.

**(Choice C)** Deformations are fetal structural anomalies that occur due to extrinsic mechanical forces. The pressure applied by the uterus is one of the most common deforming forces. For example, uterine constraint on a fetus in breech position can cause developmental dysplasia of the hip, a condition marked by abnormal development of the femoral-acetabular junction and subsequent hip instability.

**(Choice D)** Dysplasia describes abnormal organization of cellular architecture within a tissue.



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pressure applied by the uterus is one of the most common deforming forces. For example, uterine constraint on a fetus in breech position can cause developmental dysplasia of the hip, a condition marked by abnormal development of the femoral-acetabular junction and subsequent hip instability.

**(Choice D)** Dysplasia describes abnormal organization of cellular architecture within a tissue. Osteogenesis imperfecta, a skeletal disorder characterized by brittle bones that fracture easily, occurs with dysplasia of connective tissue due to absent or abnormal type I collagen.

**Educational objective:**

A developmental field defect describes multiple malformations that occur secondary to an embryonic disturbance in an adjoining group of cells. Holoprosencephaly is a developmental field defect characterized by a spectrum of fetal anomalies due to incomplete division of the forebrain (prosencephalon).

**References**


- Holoprosencephaly: recommendations for diagnosis and management.
- Holoprosencephaly: a survey of the entity, with embryology and fetal imaging.


Embryology Nervous System Holoprosencephaly



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A 23-year-old man with no prior history of seizure is brought to the emergency department after experiencing a generalized tonic-clonic seizure. His roommate says that the patient has had a fever and headache for the past 2 days and that today he was talking nonsensically. The patient works for a fast-food chain and occasionally smokes cigarettes on his breaks. He does not use alcohol or illicit drugs. Temperature is 38.6 C (101.5 F). MRI of the brain shows swelling of the temporal lobes. CSF analysis is most likely to reveal which of the following?

| | Glucose | Protein | Cells |
|---|---|---|---|
| A. | Normal | Increased | Increased (erythrocytes) |
| B. | Low | Increased | Increased (neutrophils) |
| C. | Normal | Increased | Increased (lymphocytes, erythrocytes) |
| D. | Low | Increased | Increased |



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most likely to reveal which of the following?

| | Glucose | Protein | Cells |
|---|---|---|---|
| A. | Normal | Increased | Increased (erythrocytes) |
| B. | Low | Increased | Increased (neutrophils) |
| C. | Normal | Increased | Increased (lymphocytes, erythrocytes) |
| D. | Low | Increased | Increased (lymphocytes) |
| E. | Normal | Increased | Normal |
| F. | Normal | Normal | Normal |

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most likely to reveal which of the following?

| | Glucose | Protein | Cells | |
|---|---|---|---|---|
| A. | ~~Normal~~ | ~~Increased~~ | ~~Increased (erythrocytes)~~ | (2%) |
| B. | ~~Low~~ | ~~Increased~~ | ~~Increased (neutrophils)~~ | (25%) |
| ✓ C. | Normal | Increased | Increased (lymphocytes, erythrocytes) | (54%) |
| D. | ~~Low~~ | ~~Increased~~ | ~~Increased (lymphocytes)~~ | (9%) |
| E. | Normal | Increased | Normal | (3%) |
| F. | Normal | Normal | Normal | (4%) |


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| Cerebrospinal fluid analysis | | | | |
|---|---|---|---|---|
| **Diagnosis** | **Cell count** | **Cell type** | **Glucose** | **Protein** |
| **Bacterial meningitis** | ↑↑ | Neutrophils | ↓ | ↑↑ |
| **Viral meningitis** | ↑ | Lymphocytes | Normal | Normal or ↑ |
| **Fungal or tuberculous meningitis** | ↑ | Lymphocytes | ↓ | ↑ |
| **Herpes encephalitis** | ↑ | Lymphocytes & erythrocytes | Normal | ↑ |
| **Guillain-Barré syndrome** | Normal | Normal | Normal | ↑ |

**Herpes simplex virus (HSV) type 1** is the most common cause of sporadic **encephalitis**. Patients usually present with acute-onset fever, headache, altered mental status, and focal neurologic deficits or seizure.


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**Herpes simplex virus (HSV) type 1** is the most common cause of sporadic **encephalitis**. Patients usually present with acute-onset fever, headache, altered mental status, and focal neurologic deficits or seizure. MRI classically shows **temporal lobe edema** as the virus enters the brain via the olfactory tract and travels to the olfactory cortex (located in the medial temporal lobe). Most patients have a "viral pattern" on cerebrospinal fluid (CSF) analysis with **lymphocytic pleocytosis**, normal glucose, and **elevated protein**. Hemorrhagic inflammation of the temporal lobes also usually causes **elevated erythrocytes** in the CSF.

**(Choice A)** Trauma from inserting the lumbar puncture needle can lead to a "traumatic tap," which is characterized by CSF evidence of normal glucose, elevated protein, and elevated erythrocytes.

**(Choice B)** Bacterial meningitis is usually associated with CSF evidence of low glucose, high protein, and a markedly elevated white blood cell count with a neutrophil predominance. Bacterial meningitis classically causes the triad of fever, neck stiffness, and altered mental state.

**(Choice D)** Tuberculous or fungal meningitis is often associated with CSF evidence of low glucose, moderately elevated protein, and lymphocytic pleocytosis. Most patients with herpes encephalitis have normal CSF glucose and elevated CSF erythrocytes.

**(Choice E)** Patients with Guillain-Barré syndrome (GBS) often have CSF protein elevations with normal


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**(Choice D)** Tuberculous or fungal meningitis is often associated with CSF evidence of low glucose, moderately elevated protein, and lymphocytic pleocytosis. Most patients with herpes encephalitis have normal CSF glucose and elevated CSF erythrocytes.

**(Choice E)** Patients with Guillain-Barré syndrome (GBS) often have CSF protein elevations with normal cell counts (albuminocytologic dissociation), which is thought to be due to increased permeability of the blood-nerve-barrier at the level of the nerve root. GBS usually presents with progressive, symmetric ascending muscle weakness, not seizures and fevers.

**Educational objective:**

Viral infections of the central nervous system are usually characterized by elevated protein, normal glucose, and an elevated white blood cell count with a lymphocytic predominance. Patients with herpes encephalitis also usually have elevated erythrocytes in the cerebrospinal fluid due to hemorrhagic inflammation of the temporal lobes.

| Pathology | Nervous System | HSV infection |
|---|---|---|
| Subject | System | Topic |

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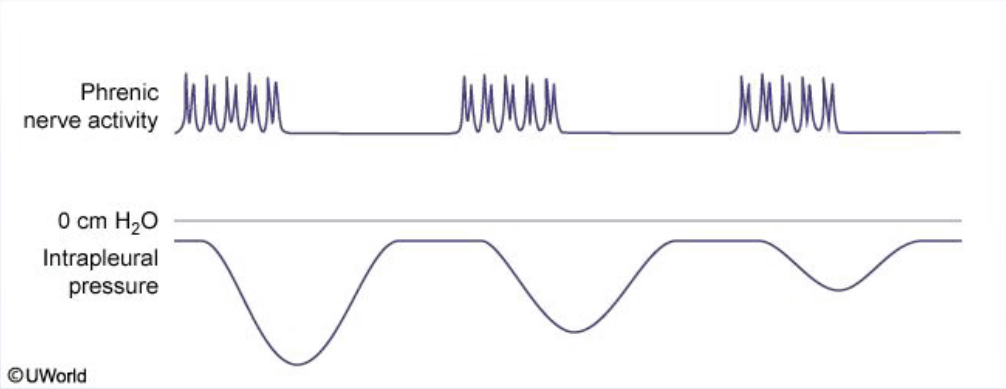
A 25-year-old woman comes to the hospital due to worsening dyspnea. The patient was previously healthy; 2 months ago, she delivered a healthy baby boy at 38 weeks gestation. Her arterial blood gas analysis shows evidence of hypoventilation. During further evaluation, she is asked to take several deep breaths, and the following physiologic information is obtained:




Which of the following locations is the most likely site of this patient's disease?

A. Brain stem

B. Nasopharynx



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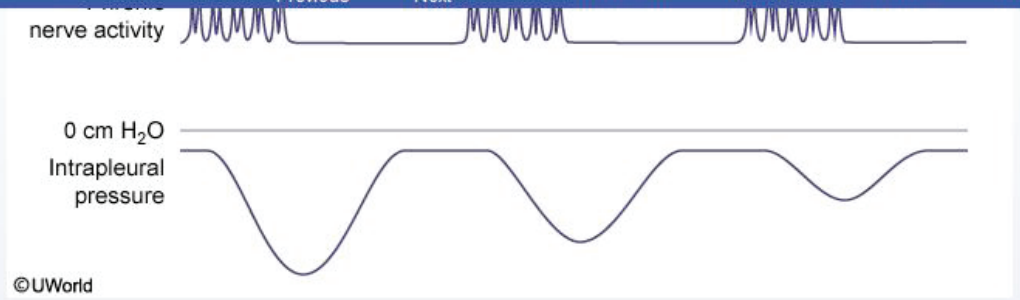


Which of the following locations is the most likely site of this patient's disease?

- A. Brain stem
- B. Nasopharynx
- C. Neuromuscular junction
- D. Pericardial space
- E. Peripheral nerves

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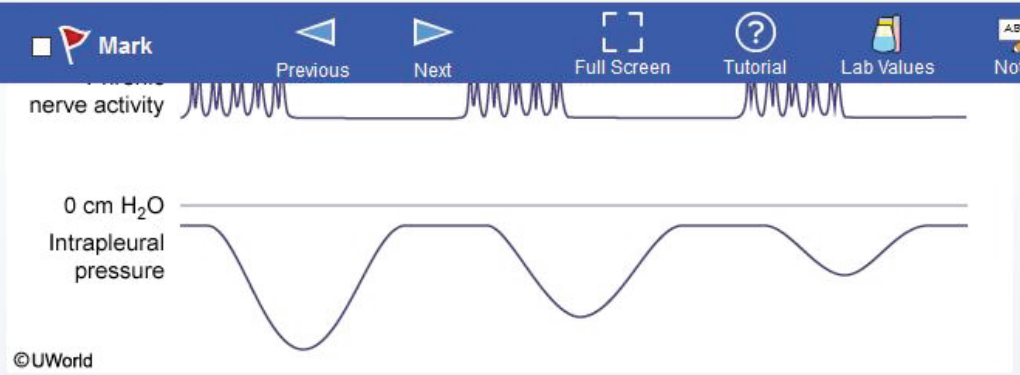


Which of the following locations is the most likely site of this patient's disease?

A. Brain stem (20%)
B. Nasopharynx (3%)
C. Neuromuscular junction (57%)
D. Pericardial space (9%)
E. Peripheral nerves (8%)

Correct
57%
59 secs
02/17/2021


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Intrapleural pressure (ie, between the lung and chest wall pleura) is slightly negative at rest due to the inward elastic recoil of the lungs and outward recoil of the chest wall. **During inspiration**, diaphragmatic contraction is primarily responsible for creating a **more negative intrapleural pressure** that causes expansion of the thoracic cavity, drawing air into the lungs. Passive expiration occurs with respiratory muscle relaxation and relies on the natural inward elastic recoil of the lungs to expel air as the intrapleural pressure returns to baseline.

The graph shows **progressive attenuation** of the intrapleural pressure change that occurs during deep, repetitive inspiration. Because there is no apparent decrement in phrenic nerve activity, this patient's progressively weaker diaphragmatic contractions are likely due to excessive skeletal muscle fatigue (eg, severe obstructive or restrictive lung disease) or impaired neuromuscular transmission. In **myasthenia gravis**, autoantibodies against postsynaptic acetylcholine receptors cause fatigable skeletal muscle weakness as **acetylcholine stores** within the presynaptic nerve terminal become progressively **depleted** with repetitive stimulation. Women in the postpartum period (like this patient) are at particularly high risk of developing myasthenia gravis.

**(Choice A)** Impairment of the respiratory control centers in the brain stem can result in decreased frequency and/or amplitude of involuntary respirations (Ondine curse). Voluntary breathing would be


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**(Choice A)** Impairment of the respiratory control centers in the brain stem can result in decreased frequency and/or amplitude of involuntary respirations (Ondine curse). Voluntary breathing would be unaffected.

**(Choice B)** Nasopharyngeal lesions are unlikely to cause inspiratory airflow obstruction severe enough to cause rapid diaphragmatic fatigue as the oropharynx remains unobstructed (allowing the patient to breath from the mouth).

**(Choices D and E)** Metastatic disease to the pericardium could compress the phrenic nerve due to its location along the pericardium. In addition, the phrenic nerve can be affected by a peripheral neuropathy. However, both diseases cause uniform weak inspirations during maximal voluntary ventilation rather than progressively weaker diaphragmatic contractions.

**Educational objective:**
Progressively weakening diaphragmatic contractions during maximal voluntary ventilation with intact phrenic nerve stimulation indicate neuromuscular junction pathology (eg, myasthenia gravis) and/or abnormally rapid diaphragmatic muscle fatigue (eg, restrictive lung or chest wall disease).

Pathophysiology Nervous System Myasthenia gravis



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A 62-year-old man is brought to the emergency department after a new-onset, generalized tonic-clonic seizure. His wife reports that for the past several weeks he has been having episodic headaches, nausea, and progressive weakness. The headaches are particularly worse at night and occasionally awaken him from sleep. His other medical problems include well-controlled hypertension and osteoarthritis. On physical examination, the patient is postictal but follows simple commands. He is admitted to the hospital for further evaluation but dies several days later due to aspiration pneumonia and septic shock. A brain section obtained during postmortem examination is shown in the image below.

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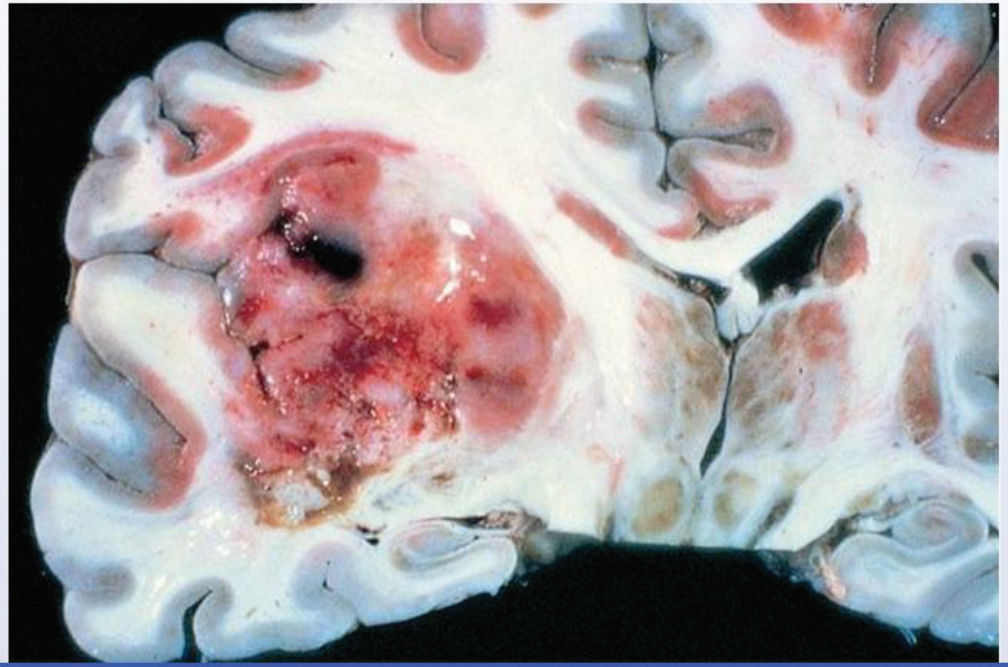



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This patient most likely had which of the following conditions?

A. Brain metastasis
B. Glioblastoma
C. Meningioma
D. Oligodendroglioma
E. Primary brain lymphoma
F. Schwannoma



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This patient most likely had which of the following conditions?

- A. ~~Brain metastasis~~ (19%)
- ✓ B. Glioblastoma (60%)
- C. ~~Meningioma~~ (5%)
- D. Oligodendroglioma (10%)
- E. ~~Primary brain lymphoma~~ (3%)
- F. ~~Schwannoma~~ (0%)

Correct

60%

01 min, 42 secs

11/27/2020



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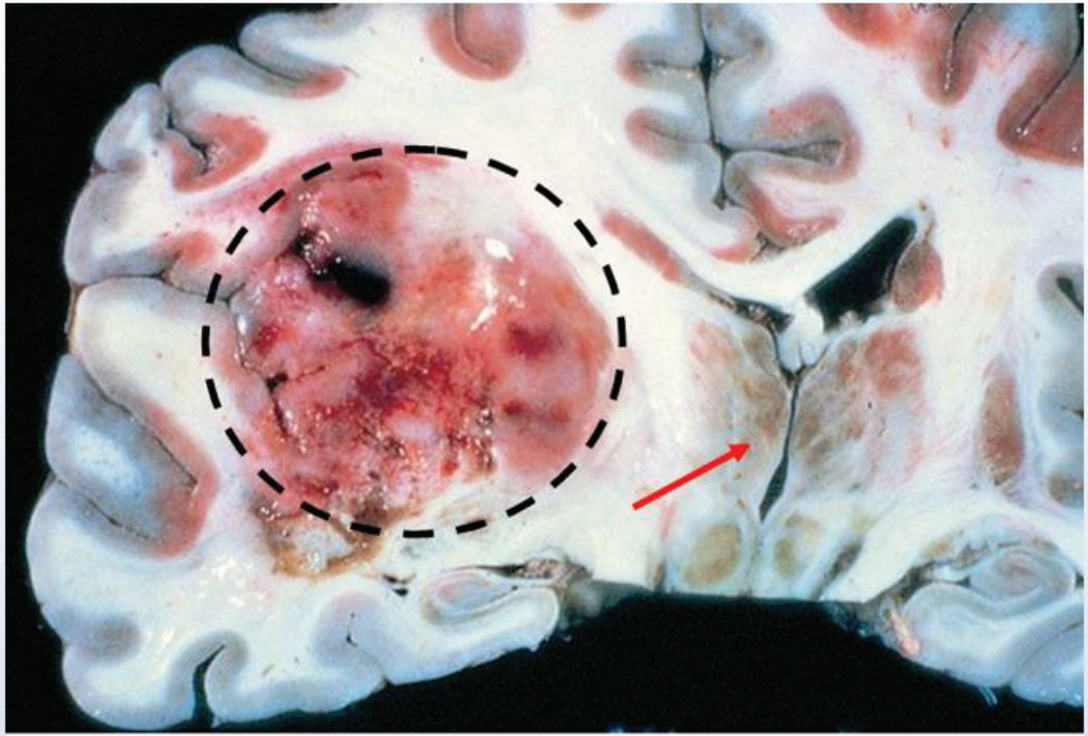

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The solitary lesion designated by the dashed circle in the image above likely represents **glioblastoma**, the most common primary cerebral neoplasm in adults. Glioblastoma arises from astrocytes and is typically located within the **cerebral hemispheres**. Tumors can become significantly large, causing mass effect with midline shift (red arrow), and may occasionally cross the corpus callosum ("butterfly glioma"). On gross examination, glioblastomas are soft and poorly defined with areas of **necrosis** and **hemorrhage**. These tumors are highly malignant with a very poor prognosis as most patients die less than a year after diagnosis.

**(Choice A)** Most adult brain tumors represent metastases from other cancers, especially those of the lung, breast, kidney, and skin (eg, melanoma). However, on gross examination, brain metastases typically appear as multiple, well-circumscribed masses at the junction of gray and white matter.

**(Choice C)** Meningiomas are benign, well-circumscribed neoplasms of adults that arise from arachnoid cells (external to the brain parenchyma). They are typically located on the brain surface at sites of dural reflection (eg, falx cerebri, tentorium cerebelli).

**(Choice D)** Oligodendrogliomas are slow growing tumors of adults that typically involve the white matter of the cerebral hemispheres. On gross examination, they usually appear as well-circumscribed gray masses with calcification.


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**(Choice D)** Oligodendrogliomas are slow growing tumors of adults that typically involve the white matter of the cerebral hemispheres. On gross examination, they usually appear as well-circumscribed gray masses with calcification.

**(Choice E)** Primary central nervous system lymphoma is most often seen in the immunocompromised (eg, patients with AIDS, transplant recipients) and appears as multiple brain lesions involving the deep gray matter, white matter, and cortex.

**(Choice F)** Schwannomas are mostly benign tumors that commonly arise from the vestibular branch of cranial nerve VIII at the cerebellopontine angle (vestibular schwannoma). Patients typically present with sensorineural hearing loss and tinnitus.

**Educational objective:**

Glioblastoma is the most common primary cerebral neoplasm of adults that is typically located within the cerebral hemispheres and may cross the midline ("butterfly glioma"). These tumors are highly malignant and grossly contain areas of necrosis and hemorrhage.

**References**

- Primary brain tumors in adults.



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A 72-year-old man is brought to the emergency department due to involuntary movements of his right arm that started several hours ago. He was watching television when his arm "threw the remote control across the room." His past medical history is significant for long-standing hypertension and diabetes mellitus. The patient does not use alcohol, tobacco, or illicit drugs. Physical examination shows wild, large-amplitude, flinging movements affecting the proximal muscles of his right arm. Which of the following areas of the brain is most likely injured in this patient?

A. Caudate nucleus
B. Internal capsule
C. Lentiform nucleus
D. Substantia nigra
E. Subthalamic nucleus
F. Ventral posterior thalamus

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A 72-year-old man is brought to the emergency department due to involuntary movements of his right arm that started several hours ago. He was watching television when his arm "threw the remote control across the room." His past medical history is significant for long-standing hypertension and diabetes mellitus. The patient does not use alcohol, tobacco, or illicit drugs. Physical examination shows wild, large-amplitude, flinging movements affecting the proximal muscles of his right arm. Which of the following areas of the brain is most likely injured in this patient?

- A. Caudate nucleus (22%)
- B. Internal capsule (5%)
- C. Lentiform nucleus (3%)
- D. Substantia nigra (6%)
- E. Subthalamic nucleus (59%)
- F. Ventral posterior thalamus (2%)



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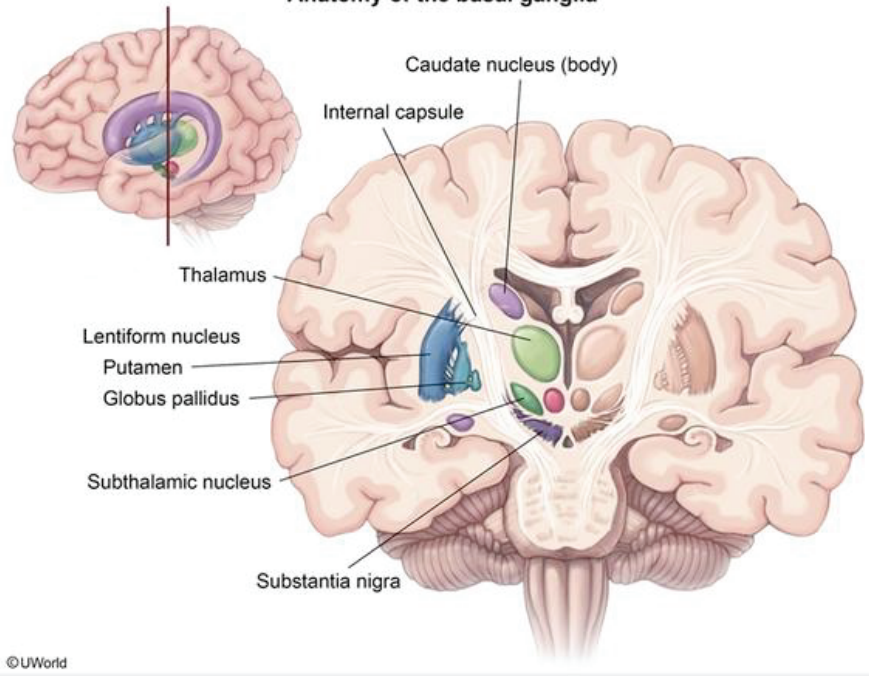
Anatomy of the basal ganglia

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The **subthalamic nucleus** is a lens-shaped structure located ventral (inferior) to the thalamus, dorsal (superior) to the substantia nigra, and medial to the internal capsule. It is a component of the **basal ganglia** and plays an important role in the modulation of basal ganglia output.

Damage to the subthalamic nucleus can decrease excitation of the globus pallidus internus, thereby reducing inhibition of the thalamus. This may result in contralateral **hemiballism**, a movement disorder characterized by wild, involuntary, large-amplitude, flinging movements involving the proximal limbs (eg, arm and/or leg) on one side of the body. This most commonly occurs in the setting of **lacunar stroke**, which is often a consequence of long-standing hypertension and diabetes mellitus.

**(Choice A)** Atrophy of the caudate nucleus occurs in Huntington disease, which is characterized by the insidious onset of chorea (involuntary, low-amplitude movements involving the distal limbs), dementia, and behavioral abnormalities.

**(Choice B)** Damage to the internal capsule may occur with lacunar infarcts, but patients typically have contralateral pure motor or combined sensorimotor deficits.

**(Choice C)** Atrophy of the lentiform nucleus (eg, globus pallidus and putamen) occurs in Wilson disease (hepatolenticular degeneration), which is characterized by liver (eg, hepatitis, cirrhosis), psychiatric (eg,



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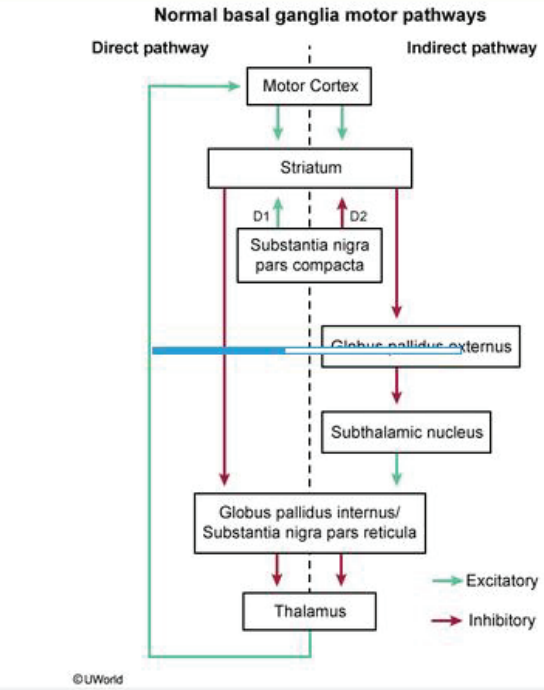


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**(Choice C)** Atrophy of the lentiform nucleus (eg, globus pallidus and putamen) occurs in Wilson disease (hepatolenticular degeneration), which is characterized by liver (eg, hepatitis, cirrhosis), psychiatric (eg, depression, personality changes), and neurologic (eg, dysarthria, movement disorder) abnormalities.

**(Choice D)** Degeneration of the substantia nigra occurs in Parkinson disease, which is characterized by bradykinesia, rigidity, and resting tremor.

**(Choice F)** Lacunar stroke involving the ventral posterior lateral nucleus and ventral posterior medial nucleus of the thalamus typically results in complete contralateral sensory loss. Damage to the thalamus may also cause thalamic syndrome, characterized by contralateral burning or stabbing pain over one side of the body.

**Educational objective:**

The subthalamic nucleus plays an important role in the modulation of basal ganglia output. Damage to this structure (eg, due to lacunar stroke) may result in contralateral hemiballism, characterized by wild, involuntary, large-amplitude, flinging movements of the proximal limbs (eg, arm and/or leg) on one side of the body.

**References**



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A 17-year-old right-handed boy is brought to the emergency department due to brief loss of consciousness after colliding with another player during a football game. The patient reports "fogginess" but has had no headache, vomiting, focal weakness or numbness, or seizures. He has no other medical conditions and takes no medications. Vital signs are within normal limits. On physical examination, the patient demonstrates retrograde amnesia about the game but no focal neurologic deficits. CT angiography of the head reveals no skull fractures or intracranial bleeding, but a small lesion in the left temporoparietal region composed of abnormal vascular channels is noted and is shown in the exhibit. Without treatment of this abnormality, which of the following will most likely occur in this patient?

A. Brain abscess
B. Flaccid paralysis
C. Malignant transformation
D. Spontaneous hemorrhage
E. Spontaneous resolution



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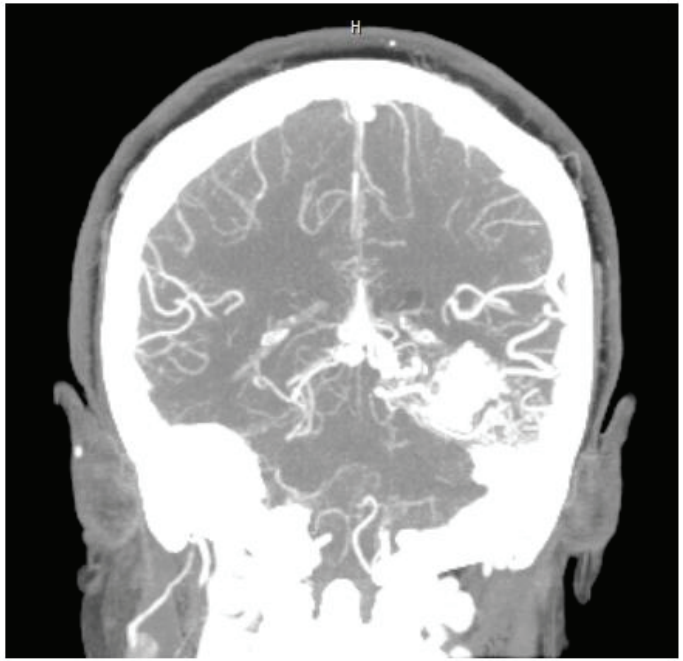


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after colliding with another player during a football game. The patient reports "fogginess" but has had no headache, vomiting, focal weakness or numbness, or seizures. He has no other medical conditions and takes no medications. Vital signs are within normal limits. On physical examination, the patient demonstrates retrograde amnesia about the game but no focal neurologic deficits. CT angiography of the head reveals no skull fractures or intracranial bleeding, but a small lesion in the left temporoparietal region composed of abnormal vascular channels is noted and is shown in the exhibit. Without treatment of this abnormality, which of the following will most likely occur in this patient?

A. Brain abscess (1%)
B. Flaccid paralysis (2%)
C. Malignant transformation (2%)
D. Spontaneous hemorrhage (85%)
E. Spontaneous resolution (8%)

Correct

85%

01 min, 21 secs

01/20/2021



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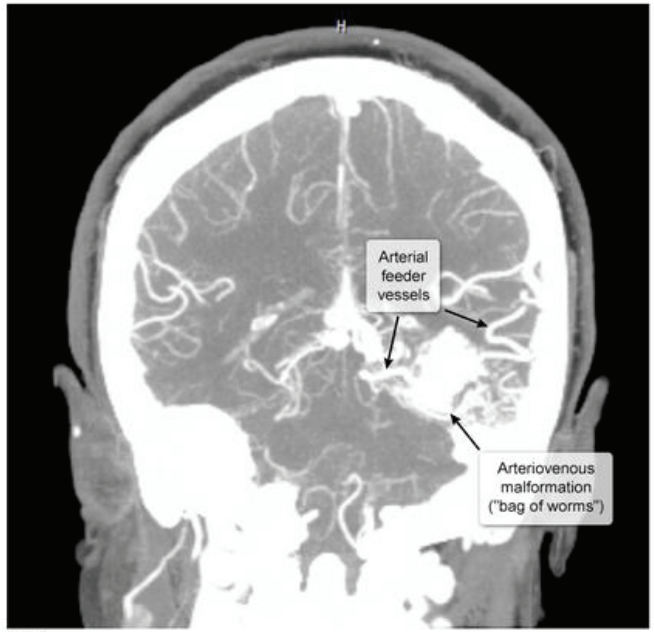
Exhibit Display

Cerebral arteriovenous malformation

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This young patient most likely sustained a concussion. Because he lost consciousness and has retrograde amnesia, imaging is performed to evaluate for intracranial hemorrhage. Incidentally, the CT angiogram reveals a cluster of dilated vessels (ie, "bag of worms") in the left temporoparietal region with large arterial feeder vessels. This is consistent with an **arteriovenous malformation** (AVM).

AVMs occur when an **artery directly anastomoses with veins** without an interposed capillary bed. The resulting high-pressure blood flow through weak vessels (ie, veins) predisposes patients to aneurysm formation and/or **spontaneous hemorrhage**. **Seizures** also commonly develop and may be due to local accumulation of hemosiderin, a cortical irritant, from microbleeds.

Most AVMs are congenital and sporadic. They can occasionally occur as a component of hereditary hemorrhagic telangiectasia (ie, Osler-Weber-Rendu syndrome), an autosomal dominant disorder associated with mucocutaneous telangiectasias (eg, nasal mucosa, intestinal mucosa) and multiorgan AVMs (eg, lungs, liver, brain).

**(Choice A)** The pulmonary capillaries filter potential debris from the venous blood (eg, clots, bacteria), preventing it from entering the systemic circulation. A pulmonary AVM (but not a cerebral AVM) bypasses this filtering system, leading to paradoxic embolization into the systemic arteries (eg, stroke or brain



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this filtering system, leading to paradoxic embolization into the systemic arteries (eg, stroke or brain abscess).

**(Choice B)** Flaccid paralysis can occur with lesions that affect the peripheral nervous system. However, lesions in the CNS lead to upper motor neuron signs (eg, spastic paralysis, hyperreflexia). In addition, cerebral AVMs very rarely lead to motor deficits.

**(Choice C)** AVMs are congenital malformations rather than neoplastic proliferations. Therefore, they are not at risk of malignant transformation.

**(Choice E)** Although some cerebral AVMs are stable and do not lead to either seizures or intracerebral hemorrhage, they never resolve spontaneously.

**Educational objective:**
Arteriovenous malformations occur when an artery directly anastomoses with veins without an interposed capillary bed. They may result in spontaneous intracerebral hemorrhage or seizures, or they may be discovered incidentally when brain imaging is obtained for another reason.

| Pathology | Nervous System | Av malformation |
|---|---|---|
| Subject | System | Topic |

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A 44-year-old man comes to the office due to hand tremors. The patient first noticed the tremor 2 years ago, and it has gradually worsened. He feels well most of the time, but his hands shake uncontrollably with activities such as pouring drinks or writing notes. The symptoms are most pronounced during stressful situations such as office meetings, and he keeps his hands tightly squeezed together or hidden below the table. He has had no arm stiffness, leg symptoms, or difficulty walking, but his wife has noticed that the patient occasionally keeps nodding his head while talking. Physical examination shows obvious tremors of outstretched hands that worsen during finger-nose testing. Which of the following additional factors is most likely to be present in this patient's medical history?

A. Exacerbation with alcohol
B. Exposure to MPTP toxin
C. Family history of tremor
D. Previous head trauma
E. Use of dopaminergic drugs



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ago, and it has gradually worsened. He feels well most of the time, but his hands shake uncontrollably with activities such as pouring drinks or writing notes. The symptoms are most pronounced during stressful situations such as office meetings, and he keeps his hands tightly squeezed together or hidden below the table. He has had no arm stiffness, leg symptoms, or difficulty walking, but his wife has noticed that the patient occasionally keeps nodding his head while talking. Physical examination shows obvious tremors of outstretched hands that worsen during finger-nose testing. Which of the following additional factors is most likely to be present in this patient's medical history?

- A. Exacerbation with alcohol (8%)
- ✗ B. Exposure to MPTP toxin (12%)
- ✓ C. Family history of tremor (64%)
- D. Previous head trauma (5%)
- E. Use of dopaminergic drugs (9%)

Incorrect
Correct answer

64%

33 secs

12/15/2020



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| Essential tremor | |
|---|---|
| **Epidemiology** | • Family history often present<br>• Up to 5% of population affected |
| **Clinical features** | • Action tremor (eg, hands outstretched)<br>• Usually bilateral<br>• Hands > arms > head >> legs<br>• Worsens with stress, improves with alcohol |
| **Treatment** | • Beta blockers: propranolol<br>• Anticonvulsants: primidone |

This patient has a worsening tremor of his distal upper extremities that becomes more pronounced with extension of his arms and at the end of an intended action (finger-to-nose test). In association with a head tremor (eg, repetitive nodding) and absence of other neurologic manifestations, this is most consistent with **essential tremor** (ET). ET is often hereditary and can be passed in an autosomal dominant fashion, so a **family history** of tremor supports the diagnosis.

Although features of ET are highly variable, it most often affects the **wrists and hands**, especially when the


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Although features of ET are highly variable, it most often affects the **wrists and hands**, especially when the arms are extended. It worsens with movement (ie, **action tremor**) and improves, but may not completely abate, at rest. Although ET is not typically unilateral, it may be asymmetric. It can also affect the **head** and voice, but it generally spares the trunk and legs and is not associated with other neurologic manifestations. Although ET does not shorten life, it is slowly **progressive** and may cause patients significant social embarrassment and impair activities of daily living.

**(Choice A)** ET classically improves with, rather than is exacerbated by, alcohol use.

**(Choices B and E)** Secondary parkinsonism can be induced by MPTP (a toxic substance that destroys dopaminergic neurons in the substantia nigra) or by the use of dopamine D2 receptor blocking drugs (eg, antipsychotics, antiemetics). Patients can have tremor, but it is typically most prominent at rest and improves with action. The tremor is also accompanied by other parkinsonian features such as rigidity, postural instability, and gait disturbances.

**(Choice D)** Previous head trauma can predispose to a wide range of neurologic sequelae, particularly headaches, seizures, and dementia. However, the development of isolated ET due to head trauma would be rare.

**Educational objective:**



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**(Choices B and E)** Secondary parkinsonism can be induced by MPTP (a toxic substance that destroys dopaminergic neurons in the substantia nigra) or by the use of dopamine D2 receptor blocking drugs (eg, antipsychotics, antiemetics). Patients can have tremor, but it is typically most prominent at rest and improves with action. The tremor is also accompanied by other parkinsonian features such as rigidity, postural instability, and gait disturbances.

**(Choice D)** Previous head trauma can predispose to a wide range of neurologic sequelae, particularly headaches, seizures, and dementia. However, the development of isolated ET due to head trauma would be rare.

**Educational objective:**
Essential tremor most often presents as a tremor of the hands that is suppressed at rest, exacerbated by outstretched arms, and more pronounced during goal-directed movements. It is often hereditary (autosomal dominant) and can be associated with a head tremor, but it is not associated with other neurologic symptoms.

| Pathology | Nervous System | Tremor |
|---|---|---|
| Subject | System | Topic |

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A 65-year-old man comes to the emergency department due to sudden-onset headache. The patient has had no recent falls or head trauma. Medical history includes hypertension and lung adenocarcinoma with abdominal metastasis. Initial noncontrast CT scan of the head reveals a small temporal lobe hemorrhage. Over the next 24 hours, the patient becomes progressively obtunded and develops generalized tonic-clonic seizures. Blood pressure is 190/96 mm Hg, pulse is 38/min, and respirations are 10/min with brief episodes of apnea. A repeat noncontrast CT scan of the head reveals acute hemorrhage expansion with brain herniation. Which of the following findings is most likely to be observed on this patient's repeat neurologic examination?

A. Dilated pupil
B. Horner syndrome
C. Hyperreflexia
D. Nystagmus
E. Upward gaze palsy



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- A. Dilated pupil (64%)
- B. Horner syndrome (9%)
- C. Hyperreflexia (10%)
- D. Nystagmus (6%)
- E. Upward gaze palsy (8%)

Correct

64%

01 min, 40 secs

10/13/2020



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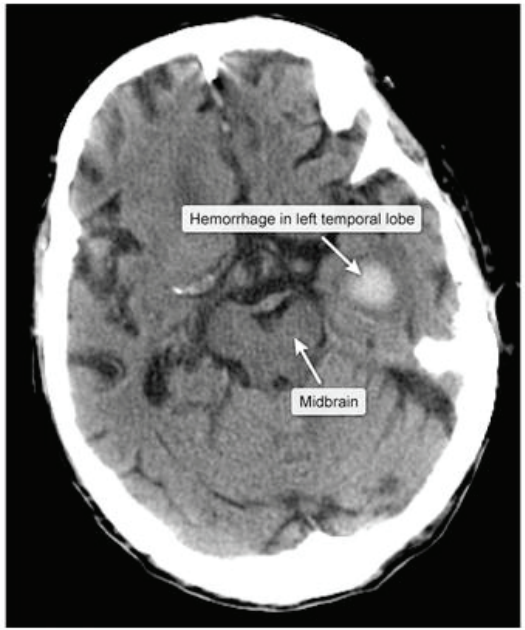
## Exhibit Display

**Left medial temporal lobe intracerebral hemorrhage**

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This patient developed a spontaneous **intracerebral hemorrhage** with subsequent clinical deterioration due to ongoing bleeding and hemorrhage expansion. Expanding space-occupying lesions (eg, hemorrhage, hematoma) **increase intracranial pressure**, which can manifest with headache, vomiting, impaired consciousness, and ultimately **Cushing triad** (eg, hypertension, bradycardia, irregular respirations) when brain herniation is imminent.

Herniation can occur in different portions of the brain depending on the location of the initial lesion. Lesions in the temporal lobe tend to cause transtentorial herniation of the uncus, which can compress the ipsilateral oculomotor nerve (CN III) as it exits the midbrain at the same level. Patients often develop ipsilateral **CN III palsy** with a fixed **dilated pupil** due to preganglionic parasympathetic nerve fiber damage.

If intracranial pressure continues to increase, the herniation can progress to involve the uncus bilaterally, ultimately causing downward displacement of the brainstem (ie, central herniation). This results in brainstem hemorrhages (ie, from rupture of paramedian basilar artery branches), continued clinical deterioration from damage to medullary cardiac and respiratory centers, abnormal posturing, and ultimately death.

**(Choice B)** Horner syndrome (ie, ptosis, miosis, anhidrosis) is associated with lesions affecting the



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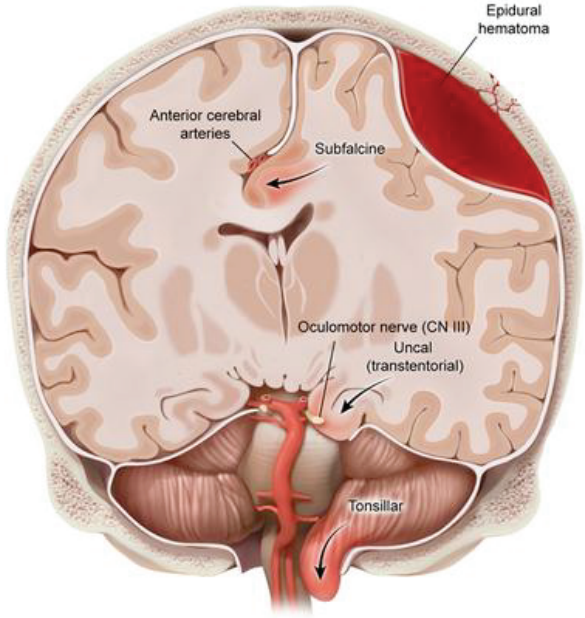
Exhibit Display

Types of brain herniation

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(Choice B) Horner syndrome (ie, ptosis, miosis, anhidrosis) is associated with lesions affecting the



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**(Choice B)** Horner syndrome (ie, ptosis, miosis, anhidrosis) is associated with lesions affecting the posterolateral hypothalamus or sympathetic tracts in the brainstem (eg, lateral medulla).

**(Choice C)** Uncal herniation can compress the cerebral peduncles, resulting in corticospinal tract injury with contralateral hemiparesis. However, patients initially have flaccid paralysis with hyporeflexia (ie, spinal shock); spasticity/hyperreflexia develops days to weeks following acute upper motor neuron injury and would not yet be present in this patient.

**(Choice D)** Nystagmus is generally seen with lesions to the pons, medulla, or cerebellum due to disruption of vestibular pathways.

**(Choice E)** Hydrocephalus can cause upward gaze palsy due to dilation of the third ventricle with compression of the dorsal midbrain (eg, superior colliculus, pretectal area).

**Educational objective:**

Expanding space-occupying lesions can increase intracranial pressure, causing transtentorial herniation of the uncus. Uncal herniation often compresses the ipsilateral oculomotor nerve (CN III) as it exits the midbrain, resulting in CN III palsy with a fixed dilated pupil (due to preganglionic parasympathetic nerve fiber damage).

**References**



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Anterior horn cells of the spinal cord of an experimental animal demonstrate cell body rounding, peripheral displacement of the nuclei and dispersion of Nissl substance to the periphery of the cells. The findings described most likely indicate:

A. Degenerative disease
B. Irreversible cell injury
C. Axonal reaction
D. Compression atrophy
E. Normal aging

Submit



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Anterior horn cells of the spinal cord of an experimental animal demonstrate cell body rounding, peripheral displacement of the nuclei and dispersion of Nissl substance to the periphery of the cells. The findings described most likely indicate:

- A. Degenerative disease (17%)
- B. Irreversible cell injury (29%)
- ✓ C. Axonal reaction (36%)
- D. Compression atrophy (8%)
- E. Normal aging (8%)

Correct

36% Answered correctly

39 secs Time Spent

01/30/2021 Last Updated

Explanation



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Sometimes axons become severed due to trauma. Such injury causes specific changes in both the proximal and distal segments of the axon, as well as in the neuronal body.

*Wallerian degeneration* occurs in the segment of axon that has lost connection with the cell body. It represents the degeneration of axon and myelin distal to a point of injury. First, swelling and irregularity are noted in the distal segment of the axon. Within a week the axon is destroyed and its fragments are digested by Schwann cells and macrophages. Similar degenerative changes occur in the segment of axon that lies proximal to the injury. Degeneration of the proximal segment extends to the closest node of Ranvier.

The changes seen in the neuronal body after the axon is severed are called ***axonal reaction.*** The cell body shows signs of cellular edema. It becomes swollen and rounded, with the nucleus displaced to the periphery. Nissl substance becomes fine, granular and dispersed throughout the cytoplasm (central chromatolysis). Axonal reaction becomes visible in 24-48 hours after the injury. Maximal changes in the neuronal body occur approximately 12 days after the injury. These changes reflect an increased synthesis of protein by the cells in order to regenerate the severed axon.

**(Choice A)** Degenerative diseases are characterized by progressive loss of neurons with associated


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**(Choice A)** Degenerative diseases are characterized by progressive loss of neurons with associated reactive glial changes. Neuronal loss in these conditions is selective: it affects one or more well-defined neuronal groups. Alzheimer's, Pick's, and Huntington's disease are all examples of degenerative disorders.

**(Choice B)** Transient but profound hypoxia, ischemia or toxic injury may lead to the loss of neurons. Irreversible neuronal injury manifests with shrinkage of the neuronal body, deep eosinophilia of the cytoplasm, pyknosis of the nucleus and loss of Nissl substance.

**(Choice D)** Compression atrophy may occur due to increased intracranial pressure or a mass lesion. A decrease in the size and number of neurons is characteristic of compression atrophy.

**(Choice E)** Normal aging is characterized by atrophy and gradual neuronal loss. Axonal reaction is not associated with this process.

**Educational Objective:**
The changes in the body of a neuron after the axon has been severed are called axonal reaction. This process reflects an increased protein synthesis that facilitates axon repair. Enlarged, rounded cells with peripherally located nuclei and dispersed finely granular Nissl substance are seen.

Pathology Nervous System Neuronal physiology


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A 15-year-old girl comes to the office with gait instability. Since age 12, the patient has had mild weakness and "clumsiness" in her lower limbs that have progressed. She has to hold on to the railing when walking down stairs due to several recent falls. Physical examination reveals kyphoscoliosis, pes cavus, and bilateral lower extremity ataxia. Joint position and vibration sense are also impaired. Further evaluation reveals that she is suffering from an inherited disease. This patient is at greatest risk of dying from which of the following conditions?

A. Aortic dissection
B. Brain tumor
C. Cardiomyopathy
D. Intracranial bleeding
E. Liver failure
F. Renal disease

Submit



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A. Aortic dissection (8%)
B. Brain tumor (4%)
✓ C. Cardiomyopathy (73%)
D. Intracranial bleeding (8%)
E. Liver failure (1%)
F. Renal disease (3%)



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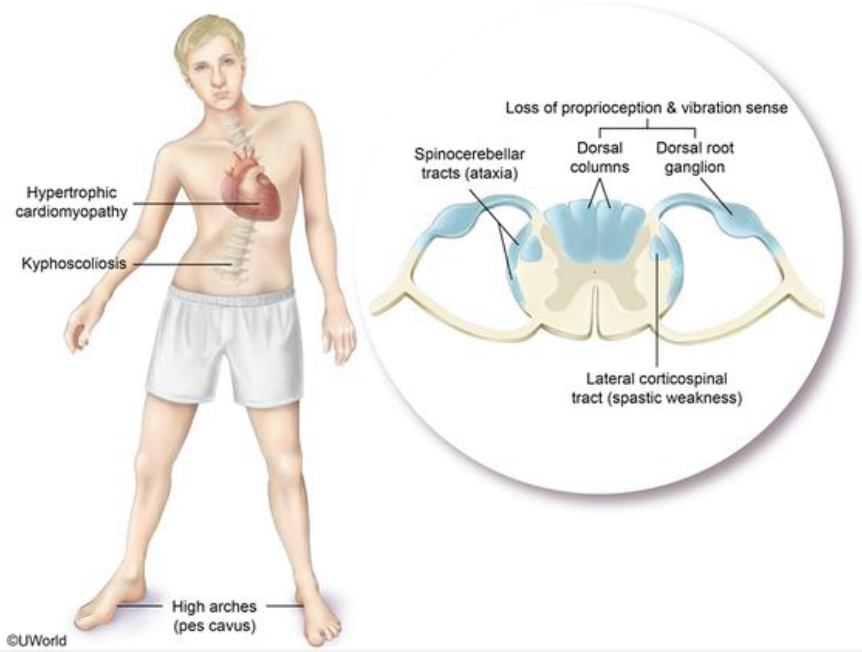
Exhibit Display

## Friedreich ataxia

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This patient likely has **Friedreich ataxia**, an autosomal recessive condition that typically presents during childhood/adolescence with progressive **gait ataxia** (due to degeneration of the spinocerebellar tracts) and impaired joint and vibration sense (due to degeneration of the posterior columns and dorsal root ganglia). Lateral corticospinal tract involvement may result in spastic muscle weakness and a positive Babinski sign.

Other characteristic features of Friedreich ataxia include **hypertrophic cardiomyopathy**, skeletal abnormalities (eg, kyphoscoliosis, pes cavus), and diabetes mellitus. Complications from cardiomyopathy (eg, cardiac arrhythmias, congestive heart failure) are the most common cause of death.

**(Choice A)** Marfan syndrome is an autosomal dominant connective tissue disorder associated with aortic dissection, mitral valve prolapse, ectopia lentis, and skeletal findings (eg, pectus excavatum, arachnodactyly, joint hypermobility).

**(Choice B)** Neurofibromatosis types 1 (NF1) and 2 (NF2) are autosomal dominant disorders. NF1 is associated with optic gliomas, whereas NF2 is associated with bilateral acoustic schwannomas and meningiomas.

**(Choices D and F)** Autosomal dominant polycystic kidney disease usually presents in adults and is associated with hypertension, renal failure, and intracranial bleeding due to ruptured Berry aneurysms.



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arachnodactyly, joint hypermobility).

**(Choice B)** Neurofibromatosis types 1 (NF1) and 2 (NF2) are autosomal dominant disorders. NF1 is associated with optic gliomas, whereas NF2 is associated with bilateral acoustic schwannomas and meningiomas.

**(Choices D and F)** Autosomal dominant polycystic kidney disease usually presents in adults and is associated with hypertension, renal failure, and intracranial bleeding due to ruptured Berry aneurysms.

**(Choice E)** Wilson disease (hepatolenticular degeneration) is an autosomal recessive disorder associated with liver failure, movement abnormalities, and psychiatric symptoms.

**Educational objective:**
Friedreich ataxia is an autosomal recessive condition that presents during childhood/adolescence with progressive gait ataxia (due to degeneration of the spinocerebellar tracts) and impaired joint and vibration sense (due to degeneration of the posterior columns and dorsal root ganglia). Other features include hypertrophic cardiomyopathy (most common cause of death), skeletal abnormalities (eg, kyphoscoliosis, pes cavus), and diabetes mellitus.

**References**

- Clinical features of Friedreich's ataxia: classical and atypical phenotypes


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A 56-year-old man is brought to the emergency department due to progressive weakness and lethargy. The patient has also had a nonproductive cough for the past several weeks. He has no prior medical conditions and takes no medications. He has smoked a pack of cigarettes daily for 30 years. Physical examination shows no abnormalities. Chest x-ray reveals a lung mass. Further evaluation reveals an electrolyte abnormality induced by ectopic antidiuretic hormone production from a lung mass. This patient is at greatest risk of which of the following conditions if his electrolyte abnormality is corrected too quickly?

A. Cardiac arrhythmias
B. Cerebral demyelination
C. Cerebral edema
D. Diffuse myonecrosis
E. Intravascular hemolysis

Submit



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A 56-year-old man is brought to the emergency department due to progressive weakness and lethargy. The patient has also had a nonproductive cough for the past several weeks. He has no prior medical conditions and takes no medications. He has smoked a pack of cigarettes daily for 30 years. Physical examination shows no abnormalities. Chest x-ray reveals a lung mass. Further evaluation reveals an electrolyte abnormality induced by ectopic antidiuretic hormone production from a lung mass. This patient is at greatest risk of which of the following conditions if his electrolyte abnormality is corrected too quickly?

- A. Cardiac arrhythmias (4%)
- ✓ B. Cerebral demyelination (78%)
- C. Cerebral edema (15%)
- D. Diffuse myonecrosis (0%)
- E. Intravascular hemolysis (0%)

Correct

78% Answered correctly

52 secs Time Spent

02/20/2021 Last Updated



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This patient's **ectopic antidiuretic hormone** production is likely to cause **chronic hyponatremia** due to excessive resorption of free water by the kidneys. Decreased serum tonicity causes water to cross the blood brain barrier and enter the central nervous system. In response to cellular swelling, brain cells excrete osmolytes (organic solutes [glutamate, myoinositol], electrolytes), resulting in intracellular water loss and normalization of brain volume.

**Overly rapid correction** of chronic hyponatremia can cause **osmotic demyelination syndrome** (also known as central pontine myelinolysis). A rapid increase in extracellular tonicity (eg, due to aggressive saline hydration) quickly draws water out of central nervous system cells. The resulting uncontrolled cell shrinkage leads to degeneration of astrocytes (crucial for myelin maintenance) and oligodendrocytes. Demyelination typically affects the **pons**, but can also occur at extrapontine sites (eg, basal ganglia and **cerebral white matter**).

Clinical features typically become apparent within 2-6 days. Features may include **spastic quadriplegia** (corticospinal tract involvement) and **pseudobulbar palsy** (dysphagia, dysarthria, tongue paresis). Patients with involvement of the bilateral pons may develop **locked in syndrome** with near-total paralysis and aphasia but with intact cognitive abilities, blinking, and vertical eye movements.

**(Choice A)** Parathyroid hormone–related protein production is associated with squamous cell carcinoma


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and aphasia but with intact cognitive abilities, blinking, and vertical eye movements.

**(Choice A)** Parathyroid hormone–related protein production is associated with squamous cell carcinoma of the lung; the resultant hypercalcemia can cause cardiac arrhythmias. However, rapid correction of hypercalcemia is not associated with arrhythmias.

**(Choice C)** Cerebral edema results from rapid correction of *hypernatremia* with *hypotonic fluids* (free water flows into brain cells). This typically occurs in patients with chronic dehydration or diabetes insipidus (antidiuretic hormone deficiency or resistance), not with excessive antidiuretic hormone production.

**(Choices D and E)** Severe hypophosphatemia can occur when feeding a severely malnourished patient (refeeding syndrome). It results in ATP depletion, which can cause hemolysis and rhabdomyolysis (diffuse myonecrosis). Patients require rapid correction of the phosphorus deficiency to prevent these conditions (unlike sodium, which should be corrected slowly to prevent osmotic demyelination).

**Educational objective:**
Rapid correction of chronic hyponatremia may lead to osmotic demyelination syndrome (also known as central pontine myelinolysis). It typically manifests 2-6 days after the osmotic insult with spastic quadriplegia, pseudobulbar palsy, and locked-in syndrome.



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A 56-year-old male with history of polycystic kidney disease presented to the emergency room because of sudden onset severe headache. He has never had this type of headache in the past. Examination shows some nuchal rigidity. Neurologic examination is within normal limits. Which of the following is the most likely diagnosis?

A. Bacterial meningitis
B. Migraine headaches
C. Intracerebral hemorrhage
D. Subarachnoid hemorrhage
E. Temporal arteritis
F. Cluster headache

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A 56-year-old male with history of polycystic kidney disease presented to the emergency room because of sudden onset severe headache. He has never had this type of headache in the past. Examination shows some nuchal rigidity. Neurologic examination is within normal limits. Which of the following is the most likely diagnosis?

A. Bacterial meningitis (6%)
B. Migraine headaches (0%)
C. Intracerebral hemorrhage (6%)
D. Subarachnoid hemorrhage (84%)
E. Temporal arteritis (1%)
F. Cluster headache (1%)

Correct

84%
Answered correctly

01 min, 13 secs
Time Spent

12/09/2020
Last Updated



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Although the major pathologic process in Autosomal Dominant Polycystic Kidney Disease (ADPKD) is in the kidneys, it is a systemic disorder. Cysts and other anomalies are noted in different organs. Intracranial berry aneurysms arise in the circle of Willis, and when these aneurysms rupture they cause subarachnoid hemorrhage (SAH). The clinical presentation described in this question is suggestive of SAH. Patients complain of a severe headache ("the worst headache of their life"); neck stiffness is usually present or develops in the next 24 hours as blood in the subarachnoid space acts as a meningeal irritant. Papilledema and pupillary dilation may be noted, but there are no focal neurologic findings.

CT scan of the brain without contrast is the most commonly used initial imaging study for diagnosing SAH and should be done during the first 24 hours from the onset of symptoms. This is positive in up to 90% of patients. If the CT scan does not show SAH, but the clinical suspicion remains high, a lumbar puncture needs to be performed to evaluate the cerebrospinal fluid for the presence of xanthochromia (blood in the CSF). Thus, presence of the xanthochromia in a clinical scenario suggestive of SAH is the most sensitive test for diagnosing SAH.

**(Choice A)** The classic presentation of meningitis includes fever, headache, neck stiffness, photophobia, nausea, vomiting, and signs of cerebral dysfunction (eg, lethargy, confusion, and coma). Additionally, remember to look for clues leading you to the correct answer. For example, the question writer here mentioned that this patient has ADPKD for a reason, to lead you to SAH.


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mentioned that this patient has ADPKD for a reason, to lead you to SAH.

**(Choice B)** Migraine headache is throbbing or pulsatile. It is initially unilateral and localized in the frontotemporal and ocular area, then progresses posteriorly and becomes diffuse. It typically lasts from several hours to an entire day.

**(Choice C)** Intracerebral hemorrhage manifests with headache, vomiting and sudden onset of focal neurological deficits (hemiplegia, hemianesthesia, cranial nerve deficits, aphasia etc). Focal neurologic manifestations are unusual with SAH.

**(Choice E)** An elderly male with scalp tenderness over the temporal area (or headache), blurred vision and intermittent claudication of jaw is a typical presentation of temporal arteritis. This condition is also accompanied by a very high ESR (erythrocyte sedimentation rate) and many times occurs in the setting of polymyalgia rheumatica. Rapid treatment with corticosteroids is necessary to prevent potential blindness.

**(Choice F)** Cluster headache consists of recurrent brief attacks of sudden, severe, unilateral periorbital pain associated with ipsilateral rhinorrhea, and watering of the eyes.

**Educational Objective:**
Intracranial berry aneurysms of the circle of Willis are often seen in patients with ADPKD; when ruptured, they cause subarachnoid hemorrhage that presents with sudden onset of "thunderclap headache"


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**(Choice C)** Intracerebral hemorrhage manifests with headache, vomiting and sudden onset of focal neurological deficits (hemiplegia, hemianesthesia, cranial nerve deficits, aphasia etc). Focal neurologic manifestations are unusual with SAH.

**(Choice E)** An elderly male with scalp tenderness over the temporal area (or headache), blurred vision and intermittent claudication of jaw is a typical presentation of temporal arteritis. This condition is also accompanied by a very high ESR (erythrocyte sedimentation rate) and many times occurs in the setting of polymyalgia rheumatica. Rapid treatment with corticosteroids is necessary to prevent potential blindness.

**(Choice F)** Cluster headache consists of recurrent brief attacks of sudden, severe, unilateral periorbital pain associated with ipsilateral rhinorrhea, and watering of the eyes.

**Educational Objective:**
Intracranial berry aneurysms of the circle of Willis are often seen in patients with ADPKD; when ruptured, they cause subarachnoid hemorrhage that presents with sudden onset of "thunderclap headache".

| Pathology | Nervous System | Subarachnoidal hemorrhage |
|---|---|---|
| Subject | System | Topic |

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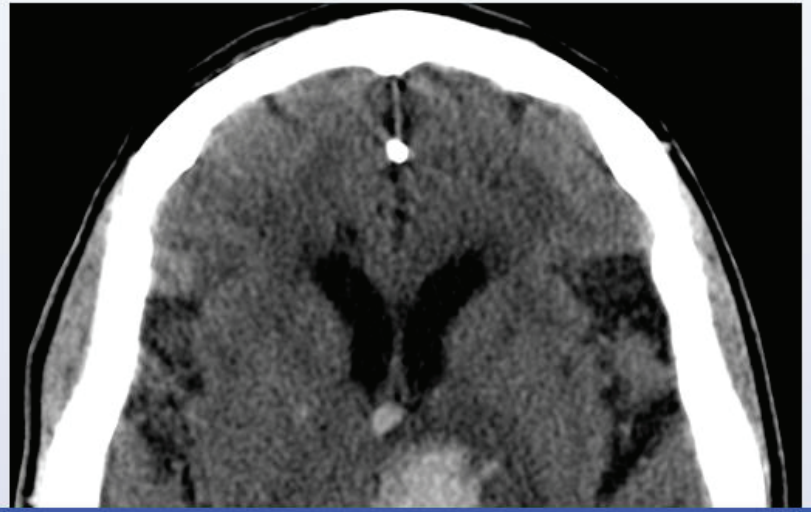
A 60-year-old professor is brought to the emergency department after developing right-sided weakness and numbness during a lecture an hour ago. He also has nausea and confusion. The patient smoked a pack of cigarettes daily for 20 years but quit 10 years ago. He does not drink alcohol. His father died of myocardial infarction at age 70. Blood pressure is 190/100 mm Hg, and pulse is 60 /min. On physical examination, there are no signs of head trauma. There is diminished right-sided strength (1/5) and an upgoing plantar reflex. Brain CT without contrast is obtained immediately. The image is shown below.





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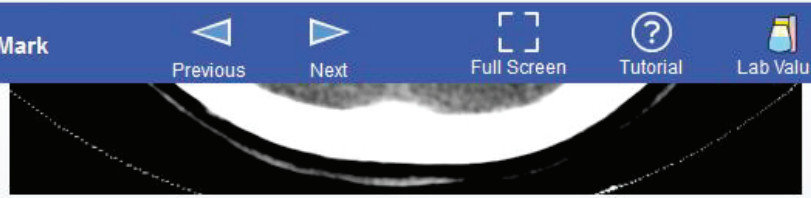

Which of the following is the most likely cause of this patient's condition?

- A. Arteriovenous malformation
- B. Cardiac embolism
- C. Carotid artery atherosclerosis
- D. Cerebral amyloid angiopathy
- E. Charcot-Bouchard aneurysm
- F. Hypertensive encephalopathy
- G. Hypoxic encephalopathy
- H. Large vessel arteritis
- I. Saccular aneurysm



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Which of the following is the most likely cause of this patient's condition?

A. Arteriovenous malformation (2%)
B. ~~Cardiac embolism~~ (4%)
C. ~~Carotid artery atherosclerosis~~ (6%)
D. ~~Cerebral amyloid angiopathy~~ (3%)
E. Charcot-Bouchard aneurysm (52%)
F. ~~Hypertensive encephalopathy~~ (16%)
G. ~~Hypoxic encephalopathy~~ (1%)
H. ~~Large vessel arteritis~~ (0%)
I. ~~Saccular aneurysm~~ (13%)

Correct

52%

01 min, 27 secs

03/05/2021



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| | Charcot-Bouchard aneurysms | Saccular (berry) aneurysms |
|---|---|---|
| **Associated conditions** | • Hypertension | • ADPKD, Ehlers-Danlos syndrome, hypertension |
| **Location** | • Basal ganglia<br>• Cerebellum<br>• Thalamus<br>• Pons | • Circle of Willis |
| **Size** | • <1 mm | • Variable, 2-25 mm |
| **Result of rupture** | • Intracerebral hemorrhage | • Subarachnoid hemorrhage |
| **Symptoms of rupture** | • Progressive neurologic deficits<br>• Headache may follow | • Sudden severe headache<br>• Focal neurologic deficits uncommon |

**ADPKD** = autosomal dominant polycystic kidney disease.

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This patient's brain CT is diagnostic for **acute hypertensive intracerebral hemorrhage** of the thalamus.

Hypertensive vasculopathy involving the small penetrating branches of the cerebral arteries is the most



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This patient's brain CT is diagnostic for **acute hypertensive intracerebral hemorrhage** of the thalamus. Hypertensive vasculopathy involving the small penetrating branches of the cerebral arteries is the most common cause of deep intracranial hemorrhage. Chronic hypertension can lead to progressive arteriolar hyalinization and fibrinoid necrosis, weakening the vessel wall and predisposing to the formation of **Charcot-Bouchard aneurysms**. Aneurysmal rupture may ultimately lead to hemorrhage within the brain.

The most common sites of intracranial hemorrhage are **deep brain structures**, such as the basal ganglia (putamen), cerebellar nuclei, thalamus, and pons. **Acute neurologic deficits** can vary depending on hemorrhage location. This patient's contralateral weakness/numbness and extensor plantar response is consistent with thalamic hemorrhage with edema/mass effect on the internal capsule. Symptoms may worsen within minutes to hours and can be associated with headache, nausea/vomiting, or decreased level of consciousness as the hematoma expands. Acute bleeding appears as **hyperattenuated**, or bright, lesions on noncontrast head CT.

**(Choices A)** Arteriovenous malformations are the most common cause of intracranial hemorrhage in children. This patient's older age makes the diagnosis less likely.

**(Choices B and C)** Carotid artery atherosclerosis and cardiac embolism are 2 common causes of



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children. This patient's older age makes the diagnosis less likely.

**(Choices B and C)** Carotid artery atherosclerosis and cardiac embolism are 2 common causes of ischemic stroke. Clinical presentation may resemble hemorrhagic stroke; however, this patient's CT findings are consistent with hemorrhage. Spontaneous hemorrhagic transformation of ischemic stroke would be rare within hours of symptom onset.

**(Choice D)** Cerebral amyloid angiopathy is the most common cause of lobar/cortical parenchymal hemorrhage, particularly in older adults. This patient's deep intracranial hemorrhage makes hypertensive vasculopathy more likely.

**(Choice F)** Hypertensive encephalopathy is characterized by a **progressive** headache and nausea/vomiting followed by nonlocalizing neurologic symptoms (eg, confusion). This patient's focal neurologic deficits and evidence of hemorrhage on CT exclude this diagnosis.

**(Choice G)** Hypoxic encephalopathy is caused by decreased oxygenation of the blood (eg, due to cardiac arrest). It most often presents with decreased consciousness (eg, coma or vegetative state); focal neurologic deficits and intracranial hemorrhage would not be seen.

**(Choice H)** Intracranial vasculitis can lead to intraparenchymal hemorrhage but is a far less common


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**(Choice G)** Hypoxic encephalopathy is caused by decreased oxygenation of the blood (eg, due to cardiac arrest). It most often presents with decreased consciousness (eg, coma or vegetative state); focal neurologic deficits and intracranial hemorrhage would not be seen.

**(Choice H)** Intracranial vasculitis can lead to intraparenchymal hemorrhage but is a far less common etiology compared to hypertensive vasculopathy.

**(Choice I)** Saccular aneurysm rupture is typically associated with subarachnoid hemorrhage as opposed to intraparenchymal hematoma. Patients usually have an abrupt onset of severe headache (thunderclap headache), and focal neurologic deficits are less common. On CT, subarachnoid hemorrhage appears as hyperattenuation of the sulci and basal cisterns.

**Educational objective:**
Deep intraparenchymal hemorrhage is most commonly caused by hypertensive vasculopathy of the small penetrating branches of the cerebral arteries (Charcot-Bouchard aneurysm rupture). This is in contrast to rupture of saccular aneurysms, which typically cause subarachnoid hemorrhage.

**References**

- Primary intracerebral hemorrhage.


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A 4-year-old boy is brought to the emergency department by his parents following a seizure. The patient has had an upper respiratory illness for the last 2 days but has no previous history of seizures. Today, he suddenly became unresponsive and his arms and legs started shaking for approximately 40 seconds. The patient was alert when the paramedics arrived at his house. In the emergency department, temperature is 40 C (104 F) and pulse is 110/min. The patient appears tired but is alert and cooperative. Physical examination shows clear nasal discharge and mild pharyngeal erythema but no nuchal rigidity or other neurologic deficits. Which of the following is the most likely underlying cause of this patient's seizure?

A. Hyperthermia-induced diffuse neuronal dysfunction
B. Microbial invasion of the meningeal layers
C. Neuronal injury from cross-reacting antiviral antibodies
D. Severe neuronal loss and gliosis in the hippocampus
E. Synchronized discharge of thalamocortical tracts

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A 4-year-old boy is brought to the emergency department by his parents following a seizure. The patient has had an upper respiratory illness for the last 2 days but has no previous history of seizures. Today, he suddenly became unresponsive and his arms and legs started shaking for approximately 40 seconds. The patient was alert when the paramedics arrived at his house. In the emergency department, temperature is 40 C (104 F) and pulse is 110/min. The patient appears tired but is alert and cooperative. Physical examination shows clear nasal discharge and mild pharyngeal erythema but no nuchal rigidity or other neurologic deficits. Which of the following is the most likely underlying cause of this patient's seizure?

- A. Hyperthermia-induced diffuse neuronal dysfunction (81%)
- B. ~~Microbial invasion of the meningeal layers~~ (4%)
- C. ~~Neuronal injury from cross-reacting antiviral antibodies~~ (8%)
- D. ~~Severe neuronal loss and gliosis in the hippocampus~~ (0%)
- E. Synchronized discharge of thalamocortical tracts (5%)

81%  01 min, 06 secs  10/18/2020



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| Febrile seizure | |
|---|---|
| **Risk factors** | • High fever (typically due to viral illness)<br>• Family history of seizures |
| **Pathophysiology** | • Circulating cytokines<br>• Hyperthermia-induced diffuse neuronal dysfunction |
| **Diagnostic criteria** | • Age 6 months to 5 years<br>• No previous afebrile seizure<br>• Absence of CNS infection/inflammation<br>• Absence of a potential metabolic cause (eg, hypoglycemia) |
| **Management** | • Symptomatic care (eg, antipyretics)<br>• Abortive therapy (if ≥5 min)<br>• Reassurance |

This patient's presentation is consistent with **febrile seizure**, a generally **benign** neurologic condition characterized by seizure and elevated temperature (≥38 C [100.4 F]) without signs of CNS infection (eg,


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This patient's presentation is consistent with **febrile seizure**, a generally **benign** neurologic condition characterized by seizure and elevated temperature (≥38 C [100.4 F]) without signs of CNS infection (eg, nuchal rigidity) or metabolic abnormality. Children age **6 months to 5 years** are almost exclusively affected because seizure threshold is lower during early years of brain development. In addition, young children are particularly susceptible to febrile **viral illnesses** (eg, roseola, influenza) associated with **high fever** (≥39.5 C [103 F]), a key risk factor for development of seizures due to **hyperthermia-induced neuronal dysfunction**.

A simple febrile seizure is characterized by a generalized seizure (eg, unresponsiveness, tonic-clonic movements) that is short (<15 min) and does not recur within 24 hours. Benzodiazepines can be used to abort seizures lasting ≥5 mins; however, most self-resolve prior to presentation. Treatment primarily involves **antipyretics** (eg, nonsteroidal anti-inflammatory drugs), which **decrease fever** by inhibiting prostaglandin $E_2$ synthesis and counteracting the effects of circulating cytokines, resulting in reduction of the thermoregulatory set point in the hypothalamus.

**(Choice B)** Microbial invasion of the meningeal layers occurs with meningitis, a serious infection that may progress to encephalitis and trigger generalized seizures. However, meningitis causes other findings not seen in this patient, such as nausea/vomiting, photophobia, nuchal rigidity, and prolonged confusion (ie



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**(Choice B)** Microbial invasion of the meningeal layers occurs with meningitis, a serious infection that may progress to encephalitis and trigger generalized seizures. However, meningitis causes other findings not seen in this patient, such as nausea/vomiting, photophobia, nuchal rigidity, and prolonged confusion (ie, persisting after post-ictal period).

**(Choice C)** Neuronal injury from cross-reacting antiviral antibodies describes acute cerebellar ataxia, which often occurs in children following a viral illness but presents with gait instability, impaired coordination, and tremor.

**(Choice D)** Severe neuronal loss and gliosis in the hippocampus (ie, hippocampal sclerosis) causes mesial temporal lobe epilepsy. Although this condition is associated with a history of childhood febrile seizures, it usually presents in young adults as focal-onset seizures (rather than generalized-onset seizures) characterized by unilateral motor symptoms, a rising epigastric sensation, and auditory/olfactory auras.

**(Choice E)** Absence seizures are initiated by synchronized slow-wave discharge of thalamocortical tracts. Although these seizures are more common in children with a history of febrile seizures, they are characterized by staring spells of <20 seconds, not unresponsiveness for 40 seconds with shaking movements.


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seizures) characterized by unilateral motor symptoms, a rising epigastric sensation, and auditory/olfactory auras.

**(Choice E)** Absence seizures are initiated by synchronized slow-wave discharge of thalamocortical tracts. Although these seizures are more common in children with a history of febrile seizures, they are characterized by staring spells of <20 seconds, not unresponsiveness for 40 seconds with shaking movements.

**Educational objective:**

Febrile seizure is usually a benign neurologic disorder that occurs most commonly in children age 6 months to 5 years who have high fever due to a viral illness. The pathophysiology involves hyperthermia-induced neuronal dysfunction triggering a short (<5 min) generalized seizure; treatment is generally supportive with antipyretics for fever reduction.

**References**

- Febrile seizures.

| Pathophysiology | Nervous System | Febrile seizure |
|---|---|---|
| Subject | System | Topic |



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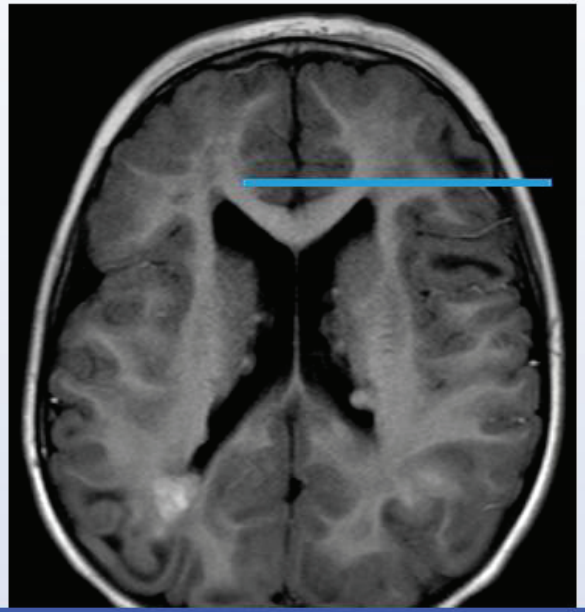
A 3-year-old boy is being evaluated for recurrent generalized seizures and developmental delay. Physical examination is notable for scattered hypopigmented skin patches. MRI of the head reveals multiple masses, most of which line the ependymal surfaces of the lateral ventricles, and some are calcified, as shown in the below image.





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Item 1 of 1
Question Id: 7605

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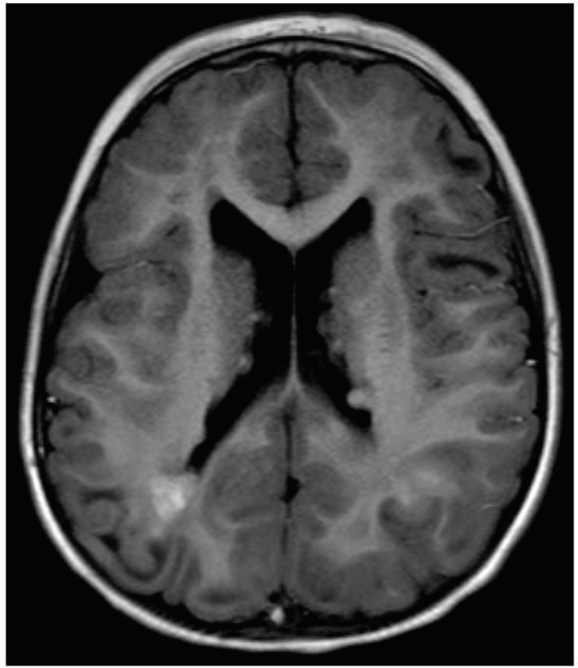

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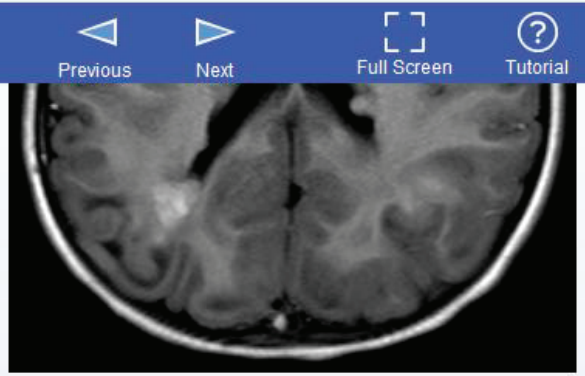

Which of the following is the most likely underlying cause of this patient's brain lesions?

A. Benign hamartoma formation
B. Lysosomal metabolite accumulation
C. Malignant lymphoid proliferation
D. Mycobacterial meningeal invasion
E. Tapeworm larvae migration

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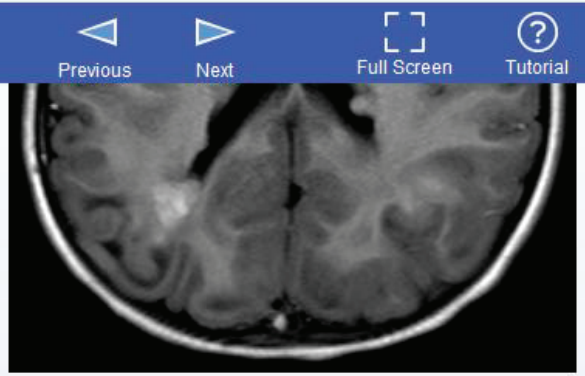

Which of the following is the most likely underlying cause of this patient's brain lesions?

- ✓ A. Benign hamartoma formation (74%)
- B. ~~Lysosomal metabolite accumulation~~ (15%)
- C. ~~Malignant lymphoid proliferation~~ (3%)
- ✗ D. Mycobacterial meningeal invasion (3%)
- E. Tapeworm larvae migration (4%)

Incorrect
Correct answer

Collecting Statistics

02 mins, 33 secs

03/20/2021



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| Tuberous sclerosis complex | |
|---|---|
| **Pathophysiology** | • Autosomal dominant<br>• Mutation in *TSC1* or *TSC2* tumor suppressor gene<br>• Defective tuberin-hamartin complex → unrestricted cellular proliferation |
| **Classic findings** | • Skin:<br>◦ Ash-leaf spots<br>◦ Facial angiofibromas<br>◦ Shagreen patches<br>• Neurologic:<br>◦ CNS hamartomas (eg, subependymal nodules)<br>◦ Seizures<br>◦ Intellectual disability<br>• Cardiac: rhabdomyomas<br>• Renal: angiomyolipomas |

This patient's findings are consistent with **tuberous sclerosis complex** (TSC), an autosomal dominant


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| | |
|---|---|
| | • Renal: angiomyolipomas |

This patient's findings are consistent with **tuberous sclerosis complex** (TSC), an autosomal dominant disorder caused by mutations in the genes coding for the tumor suppressor proteins hamartin and tuberin (ie, *TSC1* and *TSC2*). Unrestricted cellular proliferation results in the formation of **hamartomas**, or **benign** overgrowths of disorganized tissue. They develop primarily in the skin and CNS but may involve the heart, kidneys, eyes, and gastrointestinal tract.

**Seizures** and developmental delay are often the first presenting signs of TSC. Most patients have characteristic **cortical glioneuronal hamartomas** (tubers) in the cerebral cortex and **subependymal nodules** lining the lateral ventricles, as seen on this patient's MRI. These brain hamartomas are composed of atypical glial and neuronal elements and often **calcify**.

The first dermatologic manifestation of TSC is usually **ash-leaf spots** (ie, hypopigmented macules). Other classic cutaneous findings usually develop later and can include facial angiofibromas (ie, adenoma sebaceum), periungual fibromas, and hamartomatous plaques of connective tissue (ie, shagreen patches).

**(Choice B)** Lysosomal metabolite accumulation occurs with lysosomal storage diseases (eg, Tay-Sachs, Niemann-Pick), which can cause seizures and neurologic decline. However, symmetric areas of demyelination would be expected on MRI rather than the discrete calcifications seen in this case.


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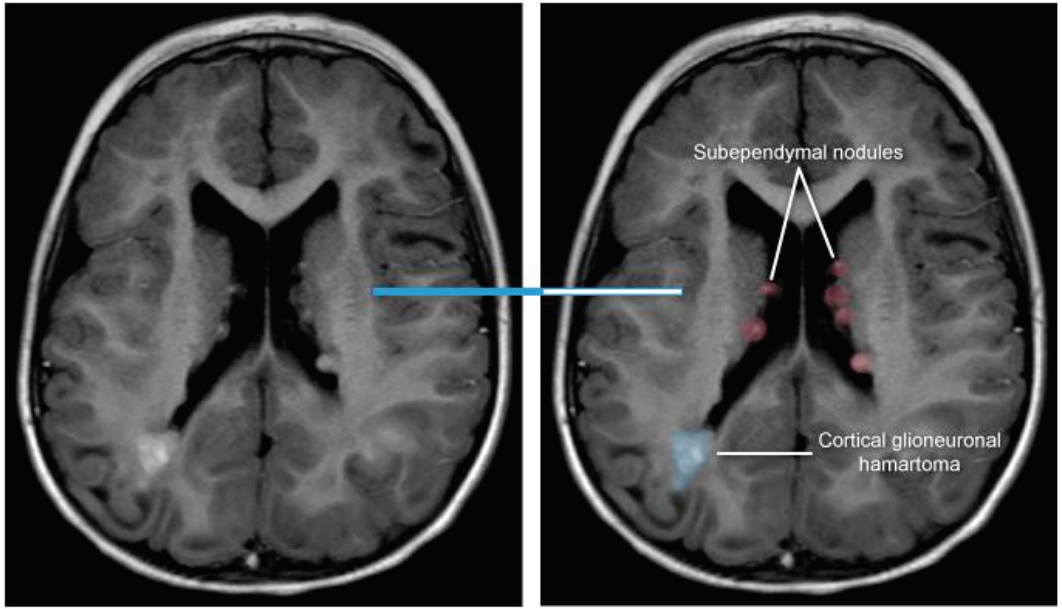
## Tuberous sclerosis complex

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demyelination would be expected on MRI rather than the discrete calcifications seen in this case.



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sebaceum), periungual fibromas, and hamartomatous plaques of connective tissue (ie, shagreen patches).

**(Choice B)** Lysosomal metabolite accumulation occurs with lysosomal storage diseases (eg, Tay-Sachs, Niemann-Pick), which can cause seizures and neurologic decline. However, symmetric areas of demyelination would be expected on MRI rather than the discrete calcifications seen in this case.

**(Choices C, D, and E)** Seizures can be the presenting sign of malignant lymphoid proliferation (ie, CNS lymphoma) or CNS infection (eg, *Mycobacterium tuberculosis*, tapeworm *Taenia solium*). However, characteristic MRI findings include ring-enhancing lesions, not subependymal nodules. Moreover, hypopigmented macules are not associated with these conditions.

**Educational objective:**
Tuberous sclerosis complex is an autosomal dominant disorder characterized by benign hamartomas of the brain (ie, cortical glioneuronal hamartomas and subependymal nodules) and skin. Seizures and ash-leaf spots are common presenting signs.

| Pathology | Miscellaneous (Multisystem) | Tuberous sclerosis |
|---|---|---|
| Subject | System | Topic |

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sebaceum), periungual fibromas, and hamartomatous plaques of connective tissue (ie, shagreen patches)

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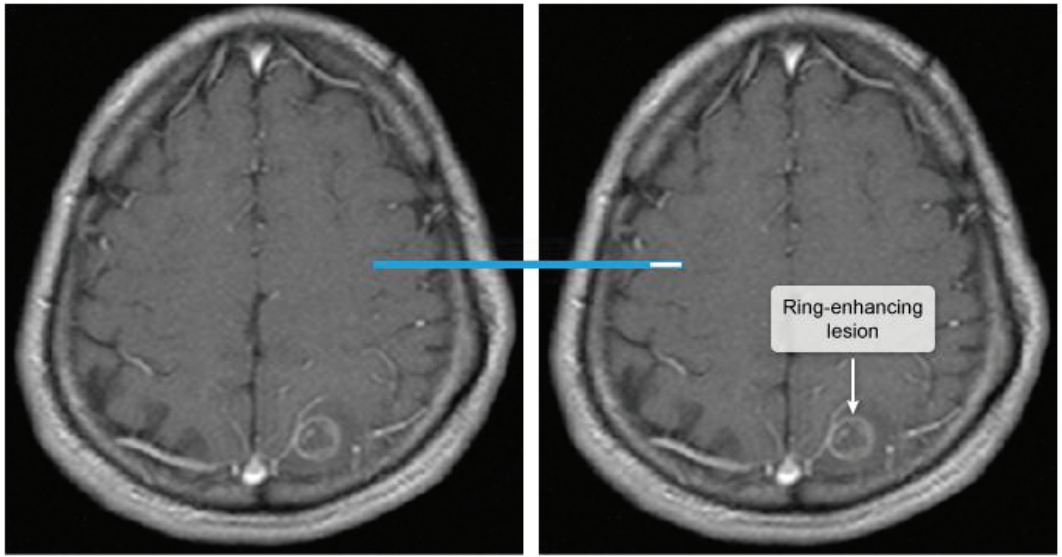
**Ring enhancing brain lesions**

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A 75-year-old woman is brought to the office by her son for evaluation of worsening forgetfulness over the past few years. She has had difficulty remembering names of the people she meets and frequently misplaces household items. Recently, the patient forgot to turn off the stove after cooking but had no major fire. She has also had disrupted sleep with frequent awakenings throughout the night. Vital signs are within normal limits. On physical examination, the patient is alert and cooperative but disoriented to time and can recall only 1 of 3 items on a short-term memory test. MRI of the head reveals diffuse cortical atrophy. A medication with which of the following effects would be most beneficial for this patient?

A. Decreased presynaptic norepinephrine reuptake
B. Decreased synaptic acetylcholine degradation
C. Increased postsynaptic NMDA receptor activity
D. Increased presynaptic dopamine synthesis
E. Increased serotonergic neurotransmission

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A 75-year-old woman is brought to the office by her son for evaluation of worsening forgetfulness over the past few years. She has had difficulty remembering names of the people she meets and frequently misplaces household items. Recently, the patient forgot to turn off the stove after cooking but had no major fire. She has also had disrupted sleep with frequent awakenings throughout the night. Vital signs are within normal limits. On physical examination, the patient is alert and cooperative but disoriented to time and can recall only 1 of 3 items on a short-term memory test. MRI of the head reveals diffuse cortical atrophy. A medication with which of the following effects would be most beneficial for this patient?

A. Decreased presynaptic norepinephrine reuptake (1%)
B. Decreased synaptic acetylcholine degradation (82%)
C. Increased postsynaptic NMDA receptor activity (8%)
D. Increased presynaptic dopamine synthesis (4%)
E. Increased serotonergic neurotransmission (2%)


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| Alzheimer disease | |
|---|---|
| **Pathogenesis** | • β-amyloid ↔ neuronal stress → excitotoxicity (glutamatergic NMDA overactivity) → neuronal degeneration → diffuse cortical atrophy<br>• Loss of cholinergic neurons → impaired memory & cognition |
| **Clinical features** | • Most common dementia; age >65 years<br>• Deficits affecting multiple cortical domains<br>◦ Memory (especially for recent events)<br>◦ Executive function (eg, planning)<br>◦ Visuospatial (eg, getting lost)<br>◦ Language (eg, poverty of speech)<br>◦ Motor (eg, gait apraxia leading to falls) |
| **Symptomatic management** | • NMDA receptor antagonist (memantine)<br>• Cholinesterase inhibitors (eg, donepezil, galantamine) |

This patient's **progressive memory loss**, functional impairments (ie, trouble with activities of daily living),


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| | |
|---|---|
| **management** | • Cholinesterase inhibitors (eg, donepezil, galantamine) |

This patient's **progressive memory loss**, functional impairments (ie, trouble with activities of daily living), and sleep disturbances are consistent with a dementia syndrome. MRI of the head reveals only **diffuse cortical atrophy** and no evidence of structural disease (eg, hydrocephalus, chronic subdural hematoma, vascular infarction). Therefore, she is most likely suffering from **Alzheimer disease** (AD), the most common form of primary dementia.

The pathogenesis of AD is complex but culminates in diffuse atrophy of cortical neurons. Specifically, **degeneration of cholinergic neurons** in the basal forebrain contributes to memory loss and functional decline. These cholinergic neurons project throughout the neocortex to positively regulate areas involved in memory (hippocampal formations) and executive function (frontal cortex), which are impaired in AD. Cholinesterase inhibitors (eg, donepezil, galantamine) block acetylcholinesterase in the synaptic cleft to compensate for the loss of cholinergic transmission.

**Cholinesterase inhibitors** have modest effects on memory and cognition to **improve daily functioning**. Cholinergic therapy should be considered in most patients with AD. Conversely, anticholinergic medications (eg, tricyclic antidepressants) should be discontinued whenever feasible because they can exacerbate cognitive dysfunction.


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exacerbate cognitive dysfunction.

Although they improve symptoms, procholinergic agents do not enhance neuron survival, so they have little impact on the overall trajectory of AD. In contrast, NMDA receptor antagonists (eg, memantine) *inhibit* glutamate NMDA signaling **(Choice C)** to prevent excitotoxicity (calcium overload) and subsequent neuronal apoptosis. These agents likely serve a neuroprotective role, slowing disease progression.

**(Choice A)** Norepinephrine-dopamine reuptake inhibitors (eg, methylphenidate, atomoxetine) are central stimulants. They can promote wakefulness to treat narcolepsy or enhance concentration to treat attention deficit hyperactivity disorder.

**(Choice D)** Dopamine precursors (eg, levodopa) can enhance dopamine availability in Parkinson disease (PD), which can be associated with dementia in later stages. They are used to improve motor rigidity but have no role in PD-related cognitive decline.

**(Choice E)** Selective serotonin reuptake inhibitors (SSRI; eg, citalopram) are first-line medications for major depressive disorder, which may mimic dementia (ie, pseudodementia). SSRIs are also used to manage the depressive mood symptoms related to AD. They do not address the underlying cognitive impairment due to neuron cell death and loss of cholinergic signaling.

**Educational objective:**


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stimulants. They can promote wakefulness to treat narcolepsy or enhance concentration to treat attention deficit hyperactivity disorder.

**(Choice D)** Dopamine precursors (eg, levodopa) can enhance dopamine availability in Parkinson disease (PD), which can be associated with dementia in later stages. They are used to improve motor rigidity but have no role in PD-related cognitive decline.

**(Choice E)** Selective serotonin reuptake inhibitors (SSRI; eg, citalopram) are first-line medications for major depressive disorder, which may mimic dementia (ie, pseudodementia). SSRIs are also used to manage the depressive mood symptoms related to AD. They do not address the underlying cognitive impairment due to neuron cell death and loss of cholinergic signaling.

**Educational objective:**

Alzheimer disease (AD) is a progressive dementia featuring diffuse cortical atrophy involving loss of cholinergic neurons. Memory, cognitive, and functional impairments of AD are partially mediated by insufficient cholinergic output. Cholinesterase inhibitors (eg, donepezil) enhance cholinergic neurotransmission to compensate for this defect.

**References**

- Alzheimer's disease: targeting the cholinergic system.



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www.ncbi.nlm.nih.gov/pubmed/26813123

A 26-year-old woman is evaluated for increasing discomfort in the right posterior mandible. The patient has no prior medical conditions and takes no medications. Physical examination is unremarkable with the exception of a partially erupted right mandibular third molar tooth. Radiographs reveal impaction of the molar tooth. Surgical tooth extraction under general anesthesia is performed. During the surgery, the inferior alveolar nerve that is close to the tooth is inadvertently injured. Which of the following is the most likely to be observed on the injured side?

A. Loss of general sensation in the anterior tongue
B. Loss of general sensation in the posterior tongue
C. Loss of sensation in the lower lip
D. Loss of taste sensation in anterior tongue
E. Loss of taste sensation in the posterior tongue
F. Weakness of the masseter muscle

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A 26-year-old woman is evaluated for increasing discomfort in the right posterior mandible. The patient has no prior medical conditions and takes no medications. Physical examination is unremarkable with the exception of a partially erupted right mandibular third molar tooth. Radiographs reveal impaction of the molar tooth. Surgical tooth extraction under general anesthesia is performed. During the surgery, the inferior alveolar nerve that is close to the tooth is inadvertently injured. Which of the following is the most likely to be observed on the injured side?

- A. Loss of general sensation in the anterior tongue (12%)
- B. Loss of general sensation in the posterior tongue (7%)
- ✓ C. Loss of sensation in the lower lip (59%)
- D. Loss of taste sensation in anterior tongue (6%)
- E. Loss of taste sensation in the posterior tongue (2%)
- F. Weakness of the masseter muscle (11%)


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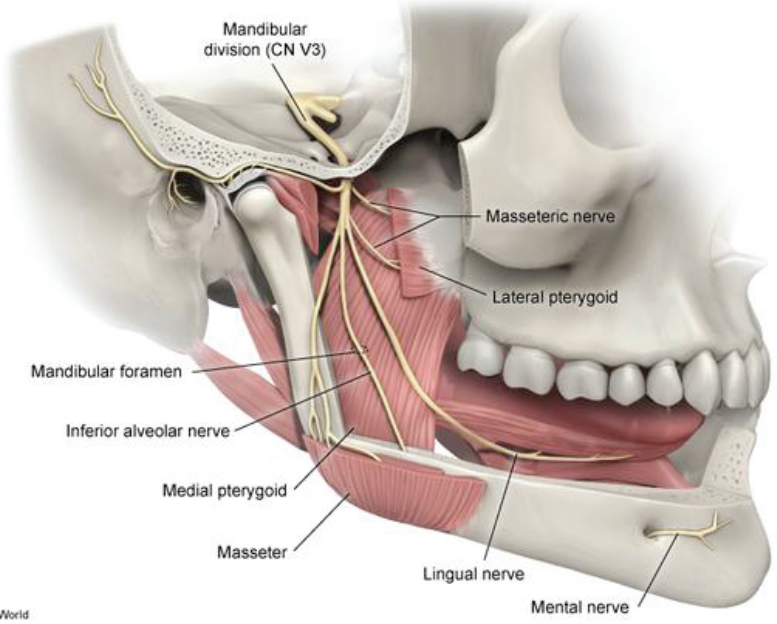
Terminal branches of the mandibular nerve

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The **inferior alveolar nerve** is a branch of the mandibular nerve (CN V3). After branching from CN V3, it enters the **mandibular foramen** to travel within the **mandibular canal**, where it can be vulnerable to iatrogenic injury during dental procedures. From inside the mandibular canal, it gives off small branches to provide sensory innervation to each of the lower teeth.

The inferior alveolar nerve also gives off the **mental nerve**, which exits the mandibular canal through the mental foramen. The mental nerve conveys sensory information from the **chin and lower lip** (both skin and mucosal surfaces). Therefore, iatrogenic injury to the inferior alveolar nerve often results in **unilateral numbness** of the lower teeth, chin, and lower lip.

Nerve blocks can be performed at the mandibular foramen to provide anesthesia for dental procedures or at the mental foramen to facilitate laceration repair of the chin and lower lip.

**(Choice A)** General sensation in the anterior tongue is carried by the lingual nerve. It is also a branch of CN V3, but it arises proximal to the inferior alveolar nerve branch. It passes between the medial pterygoid muscle and the ramus of the mandible (not into it), then through the floor of mouth where it crosses (and can be injured in procedures involving) the submandibular gland duct.

**(Choices B and E)** Both general and taste sensation in the posterior tongue are carried by the glossopharyngeal nerve (CN IX).


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The **inferior alveolar nerve** is a branch of the mandibular nerve (CN V3). After branching from CN V3, it

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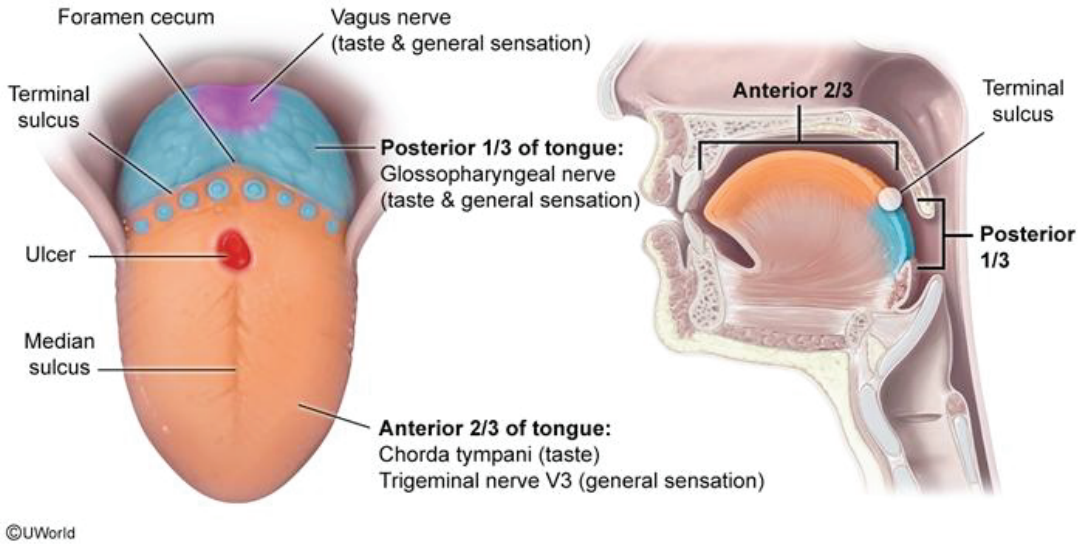
## Tongue sensory innervation

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CN V3, but it arises proximal to the inferior alveolar nerve branch. It passes between the medial pterygoid muscle and the ramus of the mandible (not into it), then through the floor of mouth where it crosses (and can be injured in procedures involving) the submandibular gland duct.

**(Choices B and E)** Both general and taste sensation in the posterior tongue are carried by the glossopharyngeal nerve (CN IX).

**(Choice D)** Taste sensation in the anterior tongue is mediated by the chorda tympani nerve, a branch of the facial nerve (CN VII) that travels with the lingual nerve.

**(Choice F)** The masseter muscle is innervated by the masseteric branch of the anterior division of the mandibular nerve (CN V3). This arises from CN V3 proximal to the branching of the inferior alveolar nerve.

**Educational objective:**
The inferior alveolar nerve travels within the mandibular canal to provide sensation to the lower teeth and can be injured during dental procedures. It gives off the mental nerve, which exits through the mental foramen to provide sensation to the chin and lower lip.

| Anatomy | Nervous System | Dental injury |
|---|---|---|
| Subject | System | Topic |

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A 26-year-old woman comes to the office due to several weeks of pain and muffled hearing in the left ear, along with a sensation of jaw clicking when chewing food. The patient has had episodic headaches and left-sided facial pain for several years that is worse when moving her jaw. She also has been told that she grinds her teeth while asleep. On examination, the patient is unable to fully open her mouth and reports pain with passive movement of the jaw. The external auditory canal and tympanic membrane are normal. A disorder affecting pterygoid muscle contractility is suspected. Involvement of which of the following nerves is most likely contributing to this patient's ear symptoms?

A. Cervical spinal nerves
B. Facial nerve
C. Mandibular nerve
D. Maxillary nerve
E. Vestibulocochlear nerve

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A 26-year-old woman comes to the office due to several weeks of pain and muffled hearing in the left ear, along with a sensation of jaw clicking when chewing food. The patient has had episodic headaches and left-sided facial pain for several years that is worse when moving her jaw. She also has been told that she grinds her teeth while asleep. On examination, the patient is unable to fully open her mouth and reports pain with passive movement of the jaw. The external auditory canal and tympanic membrane are normal. A disorder affecting pterygoid muscle contractility is suspected. Involvement of which of the following nerves is most likely contributing to this patient's ear symptoms?

A. Cervical spinal nerves (0%)
B. Facial nerve (26%)
C. Mandibular nerve (51%)
D. Maxillary nerve (12%)
E. Vestibulocochlear nerve (8%)

51%
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This patient's facial pain, headaches, jaw dysfunction, and ear pain/muffled hearing are characteristic of **temporomandibular disorder** (TMD). The underlying etiology of TMD is multifactorial but includes temporomandibular joint (TMJ) derangement (eg, jaw misalignment, trauma) and **hypersensitivity of the mandibular nerve**.

The mandibular nerve (CN V3) is the largest branch of the **trigeminal nerve** and supplies sensation to the TMJ, floor of the mouth, anterior tongue, and the lower part of the face. It also innervates the muscles of mastication (eg, medial and lateral pterygoid, masseter, temporalis), tensor veli palatini, and the tensor tympani in the middle ear, which dampens loud sounds by tensing the tympanic membrane.

Mechanical derangement of the TMJ can result in irritation and hypersensitivity of the mandibular nerve, leading to pathologic contraction of the pterygoid muscles (worsening the jaw pain and dysfunction) and tensor tympani (causing **ear pain** and **muffled hearing** despite a normal otoscopic examination).

**(Choice A)** Most patients with TMD have cervical spinal dysfunction and neck pain due to muscular and functional connections between the jaw and cervical regions. However, cervical spinal nerve damage is usually caused by overt structural lesions of the cervical spine (eg, cervical spondylosis, disc herniation) and would not result in ear pain or muffled hearing (but rather neck, shoulder, and arm pain/weakness).



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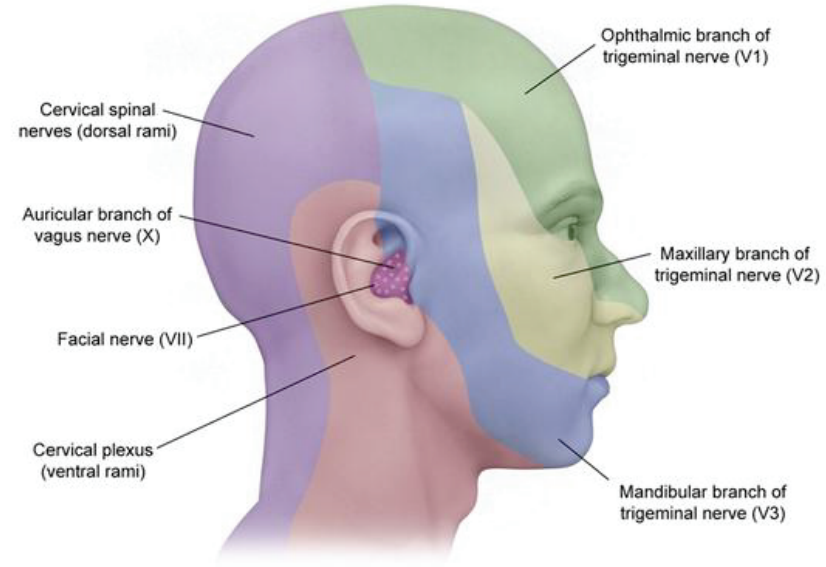
Dermatomes of head & neck

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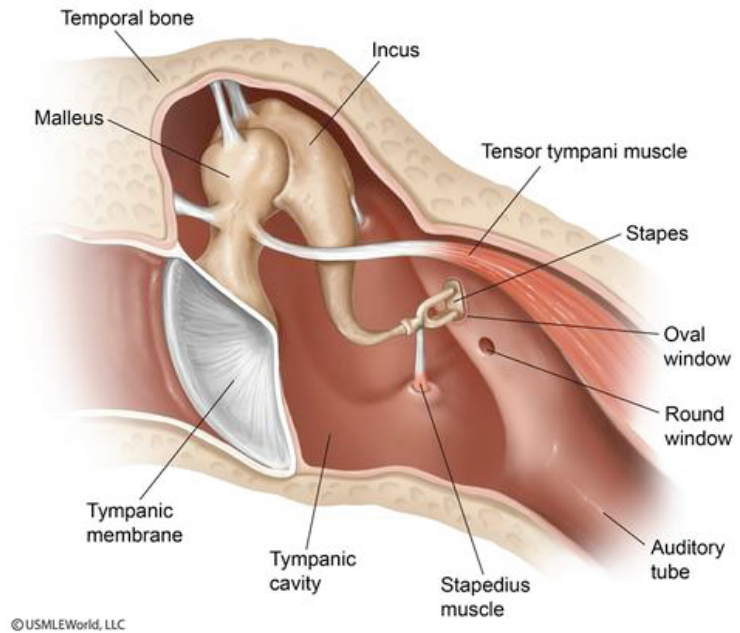
Middle ear anatomy

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**(Choice B)** The facial nerve (CN VII) provides sensory innervation to the external auditory canal/concha and motor innervation to the muscles of facial expression and the stapedius muscle, which dampens high-amplitude sound wave transmission. However, the facial nerve does not innervate the pterygoid muscles or TMJ.

**(Choice D)** The maxillary nerve (CN V2) provides sensory innervation to the cheek, nares, upper lip, and teeth. Involvement of the maxillary nerve in trigeminal neuralgia can cause facial pain; however, muffled hearing and pterygoid muscle dysfunction indicate mandibular nerve involvement.

**(Choice E)** The vestibulocochlear nerve (CN VIII) carries auditory and balance information from the inner ear. Damage to the cochlear portion of CNVIII (eg, vestibular schwannoma) can result in hearing loss; however, it would not be associated with facial pain or pterygoid muscle dysfunction.

**Educational objective:**

Temporomandibular disorder is associated with dysfunction of the temporomandibular joint and hypersensitivity of the mandibular nerve (CN V3). This can result in pathologic contraction of the pterygoid muscles (eg, jaw pain/dysfunction) and the tensor tympani in the middle ear (eg, ear pain, muffled hearing).

**References**



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A 23-year-old man is being evaluated for myoclonic epilepsy of recent onset. The episodes are short-lived and triggered by startle. Physical examination reveals proximal muscle weakness. Gomori trichrome stain of a muscle biopsy specimen shows muscle fibers with a blotchy red appearance. No family history is available because the patient is adopted. What is the probability that this patient's one offspring will inherit the disease?

- A. 100%
- B. 75%
- C. 50%
- D. 25%
- E. 0%

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A 23-year-old man is being evaluated for myoclonic epilepsy of recent onset. The episodes are short-lived and triggered by startle. Physical examination reveals proximal muscle weakness. Gomori trichrome stain of a muscle biopsy specimen shows muscle fibers with a blotchy red appearance. No family history is available because the patient is adopted. What is the probability that this patient's one offspring will inherit the disease?

A. 100% (5%)
B. 75% (2%)
C. 50% (22%)
D. 25% (14%)
✓ E. 0% (54%)

Correct

54%
Answered correctly

46 secs
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Blotchy red muscle fibers on Gomori trichrome stain are characteristic of the mitochondrial myopathies. In these conditions, abnormal mitochondria accumulate under the sarcolemma of muscle fibers. The fibers have an irregular shape and size on cross section. For this reason, the mitochondrial myopathies are also known as the "red ragged fiber" diseases. Electron microscopy of the affected muscle reveals an increased number of enlarged, abnormally shaped mitochondria.

The most important mitochondrial myopathies are myoclonic epilepsy with ragged red fibers (MERRF, described in this vignette), Leber optic neuropathy (blindness), and mitochondrial encephalopathy with stroke-like episodes and lactic acidosis (MELAS). Each of these diseases is the result of a mitochondrial gene mutation.

The mitochondrial diseases are caused by mutations, deletions or duplications of mtDNA. Because sperm mitochondria do not pass into the ovum during fertilization, only maternal mitochondria are transmitted to the fetus. Mitochondrial diseases, therefore, have maternal inheritance. For this reason the male patient described in this vignette will not transmit the disease to his progeny.

**(Choice B)** No pure single-gene inherited disease shows 75% transmission. There may be 75% transmission for a disease with variable penetrance



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described in this vignette will not transmit the disease to his progeny.

**(Choice B)** No pure single-gene inherited disease shows 75% transmission. There may be 75% transmission for a disease with variable penetrance.

Individuals affected by a disease with autosomal dominant inheritance receive one copy of the abnormal gene from one parent. The chance that an affected person will transmit the disease to his/her child is 50% **(Choice C)** if the parent is heterozygous for the given disease. If the parent is homozygous, there is a 100% chance **(Choice A)** of transmission.

**(Choice D)** Autosomal recessive diseases occur when the individual inherits two copies of the mutated gene (one from each parent). If both parents are carriers, there is a 25% chance that the child will be affected.

**Educational Objective:**
"Red ragged" muscle fibers are seen in mitochondrial diseases. Muscle fibers have this appearance because abnormal mitochondria accumulate under the sarcolemma. Mitochondrial diseases show maternal inheritance.

Genetics  Nervous System  Mitochondrial disorders


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A 2-year-old boy who recently immigrated to the United States with his family is brought to the office for irritability and excessive crying. The mother's pregnancy was uneventful, but the patient was delivered via cesarean section due to obstructed labor. His mother reports that he has developed more slowly than his brother in ability to lift his head, crawl, and walk. She has also noticed that the patient's head is larger than other children of the same age. His weight is at the 60th percentile, height is at the 50th percentile, and head circumference is at the 95th percentile. CT scan of the head is shown in the image below.

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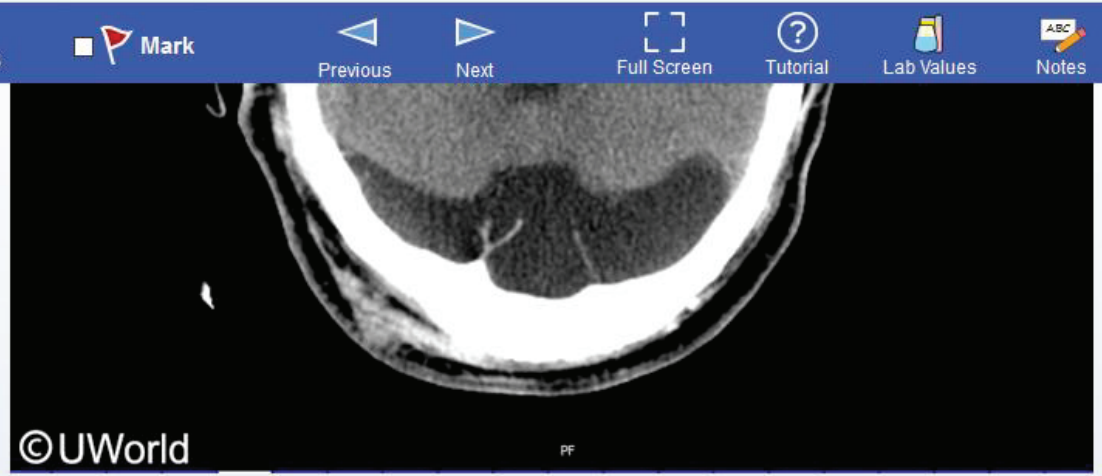


Which of the following is the most likely diagnosis?

A. Arnold-Chiari malformation
B. Arteriovenous malformation
C. Dandy-Walker malformation
D. Encephalocele
E. Hypoxic-ischemic injury



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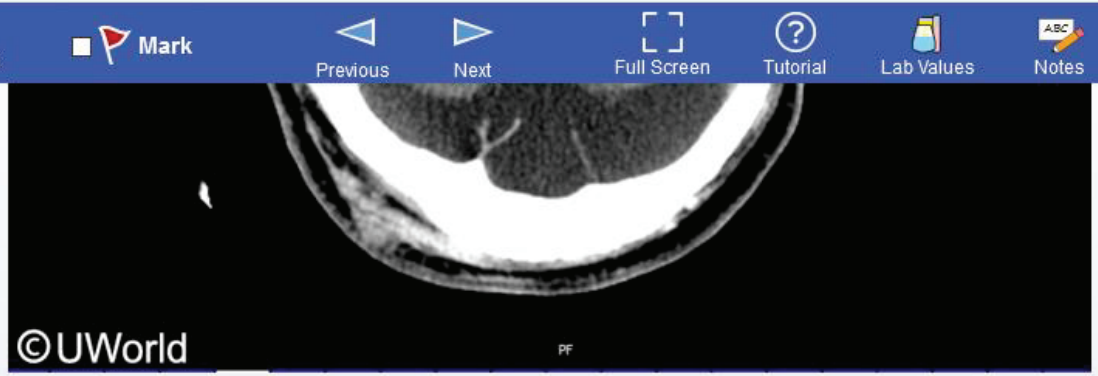


Which of the following is the most likely diagnosis?

- A. Arnold-Chiari malformation (17%)
- B. Arteriovenous malformation (5%)
- ✓ C. Dandy-Walker malformation (61%)
- D. Encephalocele (9%)
- E. Hypoxic-ischemic injury (6%)

Correct

61%

27 secs

12/21/2020



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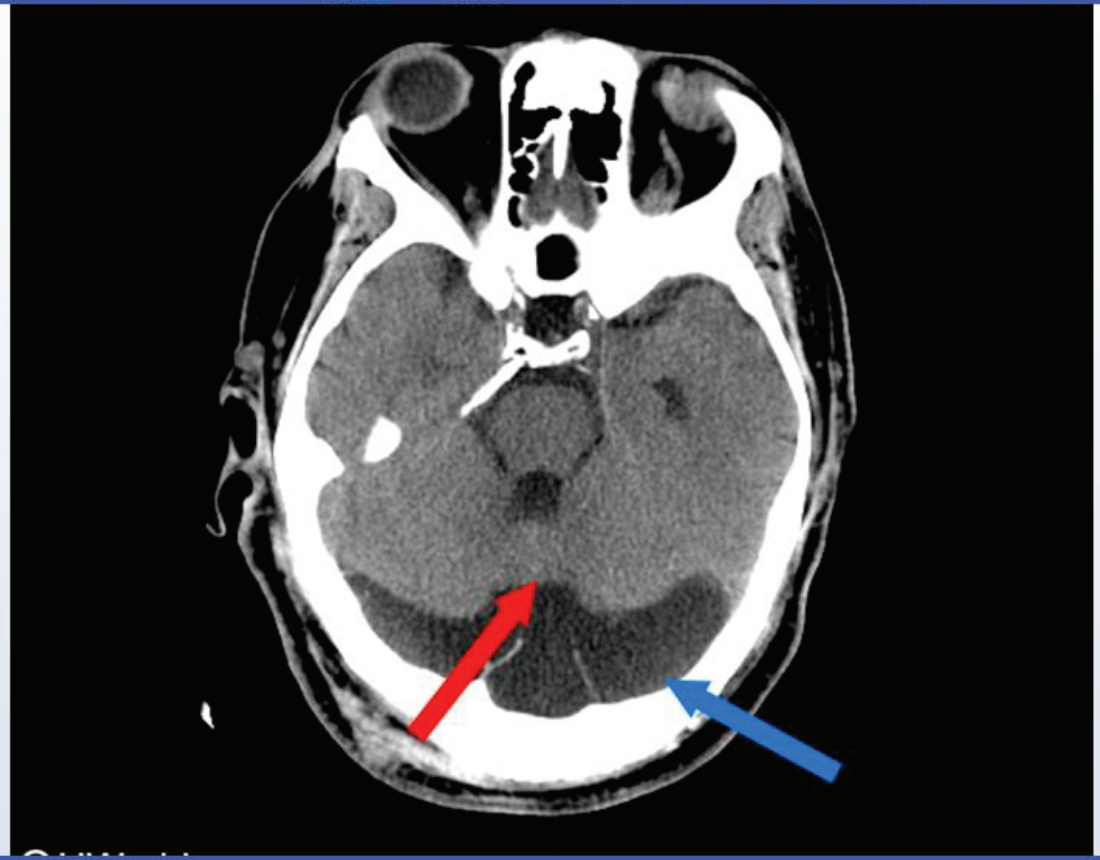



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This child likely has **Dandy-Walker malformation**, a developmental anomaly characterized by **hypoplasia/absence** of the **cerebellar vermis** (red arrow) and **cystic dilation** of the **fourth ventricle** with posterior fossa enlargement (blue arrow).

Patients often present during infancy with developmental delay and progressive skull enlargement. Cerebellar dysfunction can result in unsteadiness and impaired muscle coordination. Non-communicating **hydrocephalus** may occur due to atresia of the foramina of Luschka and Magendie, resulting in symptoms of elevated intracranial pressure (eg, irritability, vomiting). Other associated features can include agenesis of the corpus callosum and malformations involving the face, heart, or limbs.

**(Choice A)** Arnold-Chiari malformation, also known as Chiari II malformation, is characterized by downward displacement of the cerebellar vermis and tonsils below the foramen magnum. Patients also frequently have spinal myelomeningocele.

**(Choice B)** Brain arteriovenous malformations are developmental vascular lesions that usually present at age 10-30 with intracranial hemorrhage, seizure, headache, or focal neurologic deficits.

**(Choice D)** An encephalocele is a rare neural tube defect characterized by protrusion of the brain and



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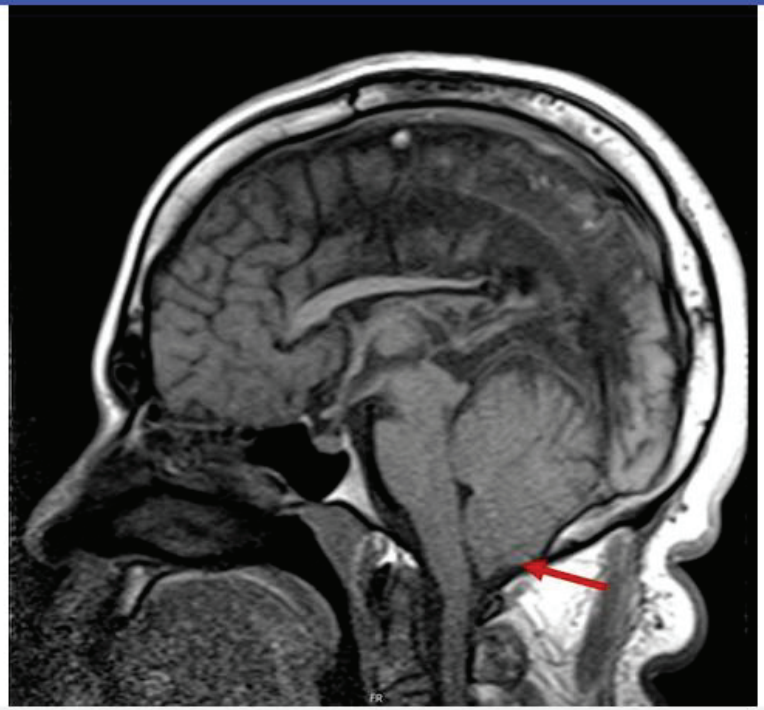

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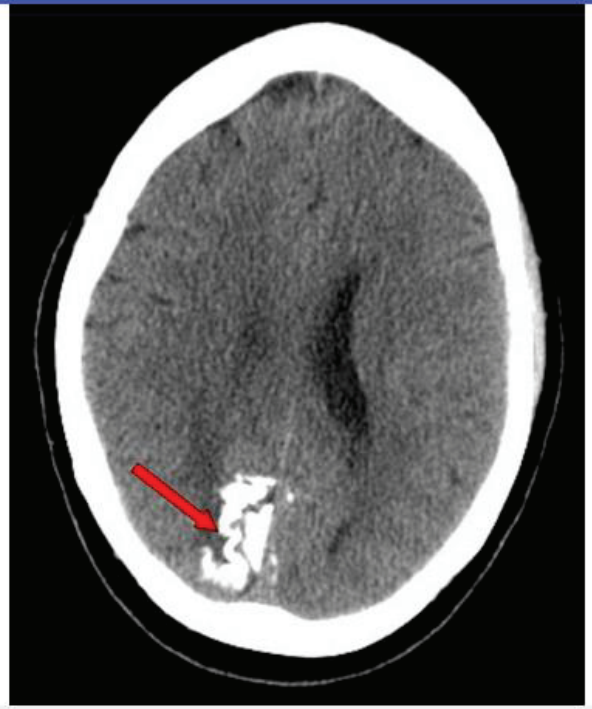

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age 10-30 with intracranial hemorrhage, seizure, headache, or focal neurologic deficits.

**(Choice D)** An encephalocele is a rare neural tube defect characterized by protrusion of the brain and meninges through an abnormal opening in the skull.

**(Choice E)** Hypoxic-ischemic brain injury may occur with complicated deliveries (eg, emergency cesarean section), but it typically presents with altered consciousness and decreased spontaneous movements during the neonatal period. Neuroimaging classically shows watershed necrosis of the gray matter between perfusion zones of the major cerebral arteries.

**Educational objective:**

Dandy-Walker malformation is a developmental anomaly characterized by hypoplasia/absence of the cerebellar vermis and cystic dilation of the fourth ventricle with posterior fossa enlargement. Patients often present during infancy with developmental delay and progressive skull enlargement. Other features may include cerebellar dysfunction and non-communicating hydrocephalus.

**References**

- Diagnosis and management of the Dandy-Walker malformation: 30 years of experience.

Pathology Nervous System Dandy walker syndrome



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Magnetic resonance imaging of the head of a young patient shows an angiomatous lesion involving the cerebellum. There is also a cystic mass in the right kidney on abdominal ultrasound. The differential diagnosis must include which of the following?

A. Neurofibromatosis type 1
B. Neurofibromatosis type 2
C. Sturge-Weber syndrome
D. Von Hippel-Lindau disease
E. Tuberous sclerosis
F. Hereditary hemorrhagic telangiectasia

Submit



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Magnetic resonance imaging of the head of a young patient shows an angiomatous lesion involving the cerebellum. There is also a cystic mass in the right kidney on abdominal ultrasound. The differential diagnosis must include which of the following?

- A. ~~Neurofibromatosis type 1~~ (2%)
- B. ~~Neurofibromatosis type 2~~ (3%)
- C. Sturge-Weber syndrome (4%)
- ✓ D. Von Hippel-Lindau disease (71%)
- E. ~~Tuberous sclerosis~~ (14%)
- F. Hereditary hemorrhagic telangiectasia (3%)

Correct

71%
Answered correctly

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Time Spent

10/04/2020
Last Updated



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| Von Hippel-Lindau disease | |
|---|---|
| **Etiology** | • Mutation in the *VHL* tumor suppressor gene on chromosome 3<br>• Autosomal dominant inheritance |
| **Manifestations** | • Cerebellar & retinal hemangioblastomas<br>• Pheochromocytoma<br>• Renal cell carcinoma (clear cell subtype) |
| **Management** | • Surveillance for associated malignancies<br>◦ Eye/retinal examination<br>◦ Plasma or urine metanephrines<br>◦ MRI of the brain & spine<br>◦ MRI of the abdomen<br>• Tumor resection |

**Von Hippel–Lindau disease** is a rare, autosomal dominant condition characterized by the presence of **capillary hemangioblastomas** in the retina and/or cerebellum, as well as congenital cysts and/or neoplasms in the kidney, liver, and pancreas. Patients are also at increased risk for renal cell carcinoma,


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**Von Hippel–Lindau disease** is a rare, autosomal dominant condition characterized by the presence of **capillary hemangioblastomas** in the retina and/or cerebellum, as well as congenital cysts and/or neoplasms in the kidney, liver, and pancreas. Patients are also at increased risk for renal cell carcinoma, which can be bilateral.

**(Choice A)** Neurofibromatosis type 1 (von Recklinghausen's disease), is an autosomal dominant disorder characterized by neurofibromas, optic nerve gliomas, Lisch nodules (pigmented nodules of the iris), and café au lait spots (hyperpigmented cutaneous macules).

**(Choice B)** Neurofibromatosis type 2 is an autosomal dominant nervous system tumor syndrome, in which patients commonly develop bilateral cranial nerve VIII schwannomas and multiple meningiomas.

**(Choice C)** Sturge-Weber syndrome (encephalotrigeminal angiomatosis) is a rare congenital neurocutaneous disorder characterized by the presence of a cutaneous facial angioma (port wine stain) as well as leptomeningeal vascular malformations. This condition is associated with intellectual disability, seizures, hemiplegia, and "tram-track" calcifications on skull radiographs.

**(Choice E)** Although tuberous sclerosis may cause kidney, liver, and pancreatic cysts, central nervous system involvement manifests not as *angiomatous* lesions, but as cortical and subependymal *hamartomas*. Renal angiomyolipomas and cardiac rhabdomyomas are also characteristic. Clinically, seizures are a


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well as leptomeningeal vascular malformations. This condition is associated with intellectual disability, seizures, hemiplegia, and "tram-track" calcifications on skull radiographs.

**(Choice E)** Although tuberous sclerosis may cause kidney, liver, and pancreatic cysts, central nervous system involvement manifests not as *angiomatous* lesions, but as cortical and subependymal *hamartomas*. Renal angiomyolipomas and cardiac rhabdomyomas are also characteristic. Clinically, seizures are a major complication.

**(Choice F)** Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome) is an autosomal dominant condition presenting with congenital telangiectasias. Rupture of these telangiectasias may cause epistaxis, gastrointestinal bleeding, or hematuria. Cysts are not characteristic.

**Educational objective:**
A cerebellar hemangioblastoma in association with congenital cysts of the kidneys, liver, and/or pancreas is highly suggestive of von Hippel–Lindau disease, a rare autosomal dominant condition.

| Pathology | Nervous System | Von hippel lindau disease |
|---|---|---|
| Subject | System | Topic |

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A 2-year-old boy with no chronic medical conditions is brought to the emergency department after he was found unresponsive with vomitus in his mouth. The patient has had muscle aches, cough, rhinorrhea, diarrhea, vomiting, and fever for the past 3 days. His parents gave him aspirin twice daily for symptom control. Vital signs are within normal limits. On examination, the patient is somnolent but withdraws from pain. Pupils are equal in size and reactive to light. Cardiopulmonary examination shows no abnormalities. Hepatomegaly is present. Extremities are well perfused. Laboratory results are as follows:

| | |
|---|---|
| Aspartate aminotransferase (SGOT) | 2,170 U/L |
| Alanine aminotransferase (SGPT) | 1,587 U/L |
| Total bilirubin | 1.7 mg/dL |
| Direct bilirubin | 1.2 mg/dL |
| Serum ammonia | 106 µmol/L (normal: 11-32) |

Over the next day, the patient's condition deteriorates and he dies despite supportive care. Examination of the brain would most likely reveal which of the following findings?

A. Diffuse astrocyte swelling



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| | |
|---|---|
| Total bilirubin | 1.7 mg/dL |
| Direct bilirubin | 1.2 mg/dL |
| Serum ammonia | 106 µmol/L (normal: 11-32) |

Over the next day, the patient's condition deteriorates and he dies despite supportive care. Examination of the brain would most likely reveal which of the following findings?

- A. Diffuse astrocyte swelling
- B. Dural venous thrombosis
- C. Hemorrhagic necrosis
- D. Inflammation of vessel walls
- E. Long-chain fatty acid deposits
- F. Pontine myelinolysis

Submit



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| | |
|---|---|
| Total bilirubin | 1.7 mg/dL |
| Direct bilirubin | 1.2 mg/dL |
| Serum ammonia | 106 µmol/L (normal: 11-32) |

Over the next day, the patient's condition deteriorates and he dies despite supportive care. Examination of the brain would most likely reveal which of the following findings?

- A. Diffuse astrocyte swelling (66%)
- B. ~~Dural venous thrombosis~~ (1%)
- C. ~~Hemorrhagic necrosis~~ (9%)
- D. ~~Inflammation of vessel walls~~ (8%)
- E. ~~Long-chain fatty acid deposits~~ (11%)
- F. Pontine myelinolysis (3%)

Correct

66%

01 min, 37 secs

03/17/2021



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| Reye syndrome | |
|---|---|
| **Pathophysiology** | • Aspirin use in children during viral infection (eg, influenza, varicella)<br>• Mitochondrial toxicity → impaired fatty acid metabolism<br>• Microvesicular fat deposits in the liver<br>• Hepatic dysfunction → hyperammonemia<br>• Diffuse astrocyte swelling (ie, cerebral edema) |
| **Clinical features** | • Acute liver failure<br>◦ Hepatomegaly<br>◦ Elevated transaminases; coagulopathy<br>• Rapidly progressive encephalopathy<br>◦ Vomiting, lethargy, seizures, coma |
| **Treatment** | • Supportive |

This patient had acute-onset **encephalopathy** and **liver failure** (eg, hepatomegaly, elevated transaminases) following the administration of aspirin for a **viral infection** (eg, influenza). These findings are characteristic of **Reye syndrome**, a rapidly progressive and potentially fatal toxic-metabolic


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This patient had acute-onset **encephalopathy** and **liver failure** (eg, hepatomegaly, elevated transaminases) following the administration of aspirin for a **viral infection** (eg, influenza). These findings are characteristic of **Reye syndrome**, a rapidly progressive and potentially fatal toxic-metabolic encephalopathy. Most cases are related to salicylates (eg, **aspirin**), which can cause **mitochondrial toxicity**, particularly when given to young children for virally-induced fever.

In the liver, impaired fatty acid oxidation by mitochondria leads to fat deposition in hepatocytes (ie, **hepatic steatosis**), hepatomegaly, and acute liver failure. In turn, excess **ammonia accumulates** due to hepatic dysfunction (eg, reduced urea cycle activity), causing **diffuse astrocyte swelling** and cerebral edema (eg, vomiting, confusion, lethargy).

Treatment of Reye syndrome is supportive. Elevated intracranial pressure (ICP), which disrupts cerebral perfusion, is a major cause of death.

**(Choice B)** Dural venous thrombosis most commonly presents with headache in young women with hypercoagulable risk factors (eg, oral contraception). Encephalopathy due to increased ICP can occur in severe cases, but liver function would not be affected. This patient's age, elevated aminotransferases, and hyperammonemia make this diagnosis unlikely.

**(Choices C and D)** Hemorrhagic necrosis of the temporal lobe is characteristic of herpes simplex virus


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severe cases, but liver function would not be affected. This patient's age, elevated aminotransferases, and hyperammonemia make this diagnosis unlikely.

**(Choices C and D)** Hemorrhagic necrosis of the temporal lobe is characteristic of herpes simplex virus encephalitis, which can present with altered mental status and focal neurologic deficits similar to those of an inflammatory CNS vasculitis. However, hepatomegaly and acute liver failure would not be expected with either condition.

**(Choice E)** Long-chain fatty acid deposition in the brain can be seen in patients with Alzheimer disease, which causes chronic dementia, not rapidly progressive encephalopathy. Although serum fatty acids can be elevated with Reye syndrome, cerebral deposition does not occur.

**(Choice F)** Pontine myelinolysis (osmotic demyelination syndrome) can cause confusion, lethargy, and coma but typically occurs with rapid correction of hyponatremia due to shifting of water out of brain cells. Liver dysfunction is not associated with this condition.

**Educational objective:**
Reye syndrome should be suspected in a young child with acute liver failure and encephalopathy after receiving aspirin for a virus-induced fever. Aspirin in this setting is a mitochondrial toxin that leads to hepatic steatosis, hyperammonemia, and diffuse astrocyte swelling (ie, cerebral edema).


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A 6-month-old girl is brought to the clinic for routine care. She has not had any illnesses, although the mother says that the girl has trouble latching when breast feeding. She can roll over when prone but cannot roll from the supine position or sit unsupported. The infant was born vaginally after an uncomplicated pregnancy. Vital signs are within normal limits. On physical examination, the girl has a head circumference above the 97th percentile for her age and a full anterior fontanelle. The remainder of her physical examination is unremarkable. At birth, the girl's head circumference was at the 50th percentile. CT scan of the head reveals significant dilation of the lateral ventricles. If this condition is left uncorrected, which of the following is the most likely complication that will be seen in this patient?

A. Infection
B. Lower extremity hyporeflexia
C. Muscle hypertonicity
D. Subarachnoid hemorrhage
E. Tumor


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mother says that the girl has trouble latching when breast feeding. She can roll over when prone but cannot roll from the supine position or sit unsupported. The infant was born vaginally after an uncomplicated pregnancy. Vital signs are within normal limits. On physical examination, the girl has a head circumference above the 97th percentile for her age and a full anterior fontanelle. The remainder of her physical examination is unremarkable. At birth, the girl's head circumference was at the 50th percentile. CT scan of the head reveals significant dilation of the lateral ventricles. If this condition is left uncorrected, which of the following is the most likely complication that will be seen in this patient?

A. Infection (4%)
B. Lower extremity hyporeflexia (20%)
C. Muscle hypertonicity (60%)
D. Subarachnoid hemorrhage (12%)
E. Tumor (1%)

Correct
60%
01 min, 11 secs
11/17/2020


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| Congenital hydrocephalus | |
|---|---|
| **Causes** | • Congenital obstruction (eg, aqueductal stenosis, Chiari malformation)<br>• Acquired obstruction (eg, congenital infection, posthemorrhagic) |
| **Symptoms** | • Macrocephaly<br>• Bulging fontanelle<br>• Poor feeding<br>• Developmental delay<br>• Spasticity & hyperreflexia |
| **Treatment** | • Cerebral shunting (ie, ventriculoperitoneal shunt) |

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**Hydrocephalus** is caused by abnormal accumulation of cerebrospinal fluid (CSF) in the brain. It is due to either overproduction or **impaired drainage** of CSF. Congenital hydrocephalus results from a structural malformation that causes impaired CSF drainage (eg, aqueductal stenosis, Chiari malformations, Dandy-Walker syndrome). Obstruction can also be secondary to infection (eg, cytomegalovirus, toxoplasmosis, meningitis) or intraventricular hemorrhage. Hydrocephalus must be distinguished from hydrocephalus ex-


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malformation that causes impaired CSF drainage (eg, aqueductal stenosis, Chiari malformations, Dandy-Walker syndrome). Obstruction can also be secondary to infection (eg, cytomegalovirus, toxoplasmosis, meningitis) or intraventricular hemorrhage. Hydrocephalus must be distinguished from hydrocephalus ex-vacuo, which is normal CSF expansion following cerebral volume loss rather than abnormal CSF accumulation.

Infants with hydrocephalus typically develop **macrocephaly**, poor feeding, **muscle hypertonicity**, and hyperreflexia. Hypertonicity and hyperreflexia result from **upper motor neuron injury** caused by stretching of the periventricular pyramidal tracts. Untreated hydrocephalus can lead to developmental delay and seizures. Treatment requires surgical placement of a **shunt** to bypass the obstruction, most often via the ventriculoperitoneal route.

**(Choices A, D, and E)** Infection, hemorrhage, and cancer do not result from hydrocephalus but are instead potential causes of acquired hydrocephalus.

**(Choice B)** Lower extremity hyporeflexia would result from damage to the lower motor neurons, which can occur in poliomyelitis or spinal muscular atrophy.

**Educational objective:**
Hydrocephalus in infants presents with macrocephaly and poor feeding. Imaging studies showing enlarged


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hyperreflexia. Hypertonicity and hyperreflexia result from **upper motor neuron injury** caused by stretching of the periventricular pyramidal tracts. Untreated hydrocephalus can lead to developmental delay and seizures. Treatment requires surgical placement of a **shunt** to bypass the obstruction, most often via the ventriculoperitoneal route.

**(Choices A, D, and E)** Infection, hemorrhage, and cancer do not result from hydrocephalus but are instead potential causes of acquired hydrocephalus.

**(Choice B)** Lower extremity hyporeflexia would result from damage to the lower motor neurons, which can occur in poliomyelitis or spinal muscular atrophy.

**Educational objective:**
Hydrocephalus in infants presents with macrocephaly and poor feeding. Imaging studies showing enlarged ventricles are characteristic. Untreated hydrocephalus leads to spasticity due to stretching of the periventricular pyramidal tracts, developmental delays, and seizures.

| Pathophysiology | Nervous System | Hydrocephalus |
|---|---|---|
| Subject | System | Topic |

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A 20-year-old man comes to the office for evaluation of abnormal behavior. Over the past 4 months, the patient has had several episodes of unresponsiveness, during which he would stare blankly while smacking his lips. He spontaneously becomes responsive after about 2 minutes and has no recollection of the event. The patient says these episodes are often preceded by an uneasy sensation in his upper abdomen and the pungent smell of something burning. He has had no falls or jerky movements of the extremities. The patient has no history of recent fever, headaches, head trauma, nausea, vomiting, or focal neurologic deficit. He had seizures in early childhood precipitated by high fevers but has had none since then and reports no other medical conditions. Cranial nerve examination reveals no abnormalities. Motor strength, sensation, and deep tendon reflexes are normal throughout. Neuroimaging is most likely to reveal an abnormality in which of the following locations in the brain?

A. Cerebellar vermis
B. Hippocampus
C. Nondominant parietal lobe
D. Occipital pole
E. Premotor frontal cortex


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patient has had several episodes of unresponsiveness, during which he would stare blankly while smacking his lips. He spontaneously becomes responsive after about 2 minutes and has no recollection of the event. The patient says these episodes are often preceded by an uneasy sensation in his upper abdomen and the pungent smell of something burning. He has had no falls or jerky movements of the extremities. The patient has no history of recent fever, headaches, head trauma, nausea, vomiting, or focal neurologic deficit. He had seizures in early childhood precipitated by high fevers but has had none since then and reports no other medical conditions. Cranial nerve examination reveals no abnormalities. Motor strength, sensation, and deep tendon reflexes are normal throughout. Neuroimaging is most likely to reveal an abnormality in which of the following locations in the brain?

A. Cerebellar vermis
B. Hippocampus
C. Nondominant parietal lobe
D. Occipital pole
E. Premotor frontal cortex



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event. The patient says these episodes are often preceded by an uneasy sensation in his upper abdomen and the pungent smell of something burning. He has had no falls or jerky movements of the extremities. The patient has no history of recent fever, headaches, head trauma, nausea, vomiting, or focal neurologic deficit. He had seizures in early childhood precipitated by high fevers but has had none since then and reports no other medical conditions. Cranial nerve examination reveals no abnormalities. Motor strength, sensation, and deep tendon reflexes are normal throughout. Neuroimaging is most likely to reveal an abnormality in which of the following locations in the brain?

A. ~~Cerebellar vermis~~ (2%)

✓ B. Hippocampus (34%)

✗ C. Nondominant parietal lobe (28%)

D. ~~Occipital pole~~ (3%)

E. ~~Premotor frontal cortex~~ (30%)

Incorrect
Correct answer

34%

01 min, 40 secs

09/22/2020



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Focal seizures originate in a single hemisphere (vs generalized seizures, which originate throughout the cerebral cortex) and are subcategorized as:

- Focal aware seizures (previously simple partial seizure): Patients are aware and interactive but have symptoms corresponding to the involved area of the brain (eg, face or limb twitching/jerking - frontal lobe motor cortex, auditory/olfactory hallucinations - temporal lobe, visual phenomena - occipital lobe).
- **Focal impaired awareness seizures** (previously complex partial seizures): Patients appear awake but do not interact appropriately (eg, **blank stare**) and frequently engage in repetitive, stereotyped **automatisms** (eg, lip smacking, hand wringing, repeating words).

Focal seizures with impaired awareness are the typical manifestation of **temporal lobe epilepsy**, the most common type of recurrent seizure disorder. Seizures are often preceded by a distinctive aura (eg, **uneasy epigastric sensation**, unpleasant **olfactory hallucinations**) that localizes the origin of the epileptiform discharges to the **mesial temporal lobe** (eg, hippocampus, amygdala, parahippocampal gyrus). The disorder is usually due to underlying hippocampal sclerosis (ie, mesial temporal sclerosis), which is associated with childhood febrile seizures.

**(Choice A)** The cerebellar vermis is responsible for vestibular function, balance, and coordination. Although patients with temporal lobe epilepsy for several years can exhibit cerebellar atrophy with


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| Seizure type | Description | Preferred anticonvulsants |
|---|---|---|
| **Focal onset** (involves a single cerebral hemisphere at onset) | | |
| **Aware** | • No loss of consciousness or postictal state<br>• Motor, sensory, autonomic, or cognitive symptoms | • Carbamazepine*<br>• Lamotrigine<br>• Levetiracetam<br>• Phenytoin* |
| **Impaired awareness** | • Appears awake but consciousness is altered (eg, blank stare)<br>• Postictal state<br>• May have automatisms (eg, lip smacking) | |
| **Generalized onset** (involves both hemispheres at onset) | | |
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |
| .. | • Brief episodes of altered consciousness (eg, blank stare) | • Ethosuxamide |

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|---|---|---|
| **Aware** | • No loss of consciousness or postictal state<br>• Motor, sensory, autonomic, or cognitive symptoms | • Carbamazepine*<br>• Lamotrigine<br>• Levetiracetam<br>• Phenytoin* |
| **Impaired awareness** | • Appears awake but consciousness is altered (eg, blank stare)<br>• Postictal state<br>• May have automatisms (eg, lip smacking) | |
| **Generalized onset** (involves both hemispheres at onset) | | |
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |
| **Absence** | • Brief episodes of altered consciousness (eg, blank stare)<br>• May have automatisms<br>• Usually no postictal state | • Ethosuximide<br>• Valproic acid |

*Narrow-spectrum agents can also treat focal-onset seizures that evolve into bilateral tonic-clonic seizures.

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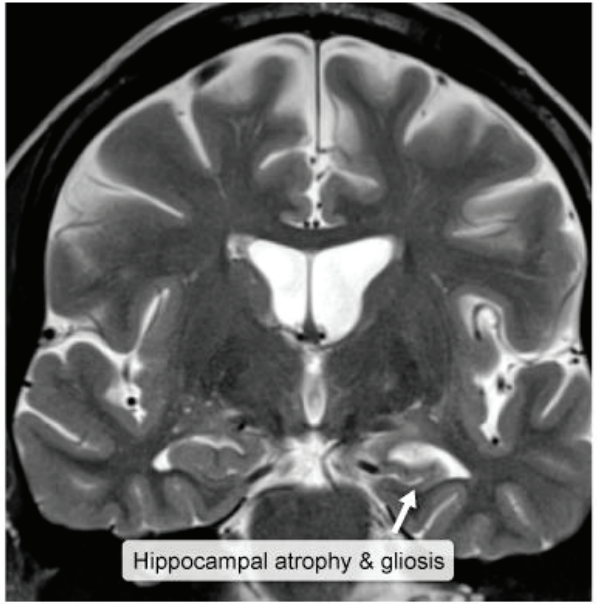
## Mesial temporal sclerosis

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Although patients with temporal lobe epilepsy for several years can exhibit cerebellar atrophy with



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associated with childhood febrile seizures.

**(Choice A)** The cerebellar vermis is responsible for vestibular function, balance, and coordination. Although patients with temporal lobe epilepsy for several years can exhibit cerebellar atrophy with accompanying ataxia, this patient has only had seizure activity for 4 months and has no evidence of ataxia on examination.

**(Choice C)** The nondominant parietal lobe plays a role in nonverbal spatial mapping and orientation. A seizure affecting this part of the brain can cause distortions in a patient's sense of position (eg, a feeling of floating, changes in posture) or visual interpretation (eg, the size of objects).

**(Choice D)** The occipital pole contains the primary visual cortex. Seizures that originate in the occipital pole characteristically have visual auras (eg, flashing lights, visual distortions, complex hallucinations).

**(Choice E)** The premotor frontal cortex is responsible for the selection of movements in response to internal and external cues. A seizure affecting this part of the brain can result in abnormal posturing or repetitive movements, but abdominal and olfactory auras would not be seen.

**Educational objective:**
Recurrent focal impaired awareness seizures that are preceded by a distinctive aura (eg, uneasy epigastric sensation, olfactory hallucinations) are characteristic of mesial temporal lobe epilepsy. The most common


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on examination.

**(Choice C)** The nondominant parietal lobe plays a role in nonverbal spatial mapping and orientation. A seizure affecting this part of the brain can cause distortions in a patient's sense of position (eg, a feeling of floating, changes in posture) or visual interpretation (eg, the size of objects).

**(Choice D)** The occipital pole contains the primary visual cortex. Seizures that originate in the occipital pole characteristically have visual auras (eg, flashing lights, visual distortions, complex hallucinations).

**(Choice E)** The premotor frontal cortex is responsible for the selection of movements in response to internal and external cues. A seizure affecting this part of the brain can result in abnormal posturing or repetitive movements, but abdominal and olfactory auras would not be seen.

**Educational objective:**
Recurrent focal impaired awareness seizures that are preceded by a distinctive aura (eg, uneasy epigastric sensation, olfactory hallucinations) are characteristic of mesial temporal lobe epilepsy. The most common etiology is hippocampal sclerosis (mesial temporal sclerosis), which is associated with childhood febrile seizures.

Pathophysiology Nervous System Seizures


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A 25-year-old woman with newly diagnosed seizures comes to the emergency department with fever and skin rash. She had her first seizure 6 weeks ago, and an MRI of the brain revealed no structural lesions. She was started on phenytoin 4 weeks ago. Her temperature is 38.9 C (102 F). There is a diffuse confluent erythema involving 60% of the body, palpable generalized lymphadenopathy, and symmetrical facial swelling. Which of the following laboratory findings is most likely to be present in this patient?

A. Antineutrophil cytoplasmic antibodies
B. Blasts cell with Auer rods
C. Cryoglobulinemia
D. Eosinophilia
E. Microangiopathic hemolytic anemia

Submit



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A 25-year-old woman with newly diagnosed seizures comes to the emergency department with fever and skin rash. She had her first seizure 6 weeks ago, and an MRI of the brain revealed no structural lesions. She was started on phenytoin 4 weeks ago. Her temperature is 38.9 C (102 F). There is a diffuse confluent erythema involving 60% of the body, palpable generalized lymphadenopathy, and symmetrical facial swelling. Which of the following laboratory findings is most likely to be present in this patient?

A. Antineutrophil cytoplasmic antibodies (18%)
B. Blasts cell with Auer rods (4%)
C. Cryoglobulinemia (11%)
✓ D. Eosinophilia (47%)
E. Microangiopathic hemolytic anemia (17%)

Correct

47%
Answered correctly

01 min, 18 secs
Time Spent

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Last Updated



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This patient's cutaneous and systemic findings after recently starting a new medication suggest drug reaction with eosinophilia and systemic symptoms **(DRESS) syndrome**. DRESS is a rare and potentially life-threatening drug reaction typically occurring 2-8 weeks after drug exposure. Commonly associated drugs include **anticonvulsants** (eg, phenytoin, carbamazepine), **allopurinol**, sulfonamides (eg, sulfasalazine), and antibiotics (eg, minocycline, vancomycin). Although the exact mechanism is unknown, it likely involves drug-induced herpesvirus reactivation followed by clonal expansion of T cells that cross-react with the drug.

Patients typically develop **fever, generalized lymphadenopathy, facial edema**, and diffuse morbilliform skin rash that can progress to a confluent erythema with follicular accentuation. Other affected organs can include the liver (hepatomegaly, jaundice), kidney (acute interstitial nephritis), and lung (cough, dyspnea). Laboratory studies usually show **eosinophilia**, atypical lymphocytosis, and elevated serum alanine transaminase. Clinical findings improve over several weeks following withdrawal of the drug.

**(Choice A)** Drug-induced antineutrophil cytoplasmic antibodies-associated vasculitis is most commonly linked to medications for hyperthyroidism (eg, propylthiouracil, methimazole) and hydralazine. Patients can develop constitutional symptoms, arthralgias/arthritis, and cutaneous vasculitis.


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**(Choice B)** Blast cells with Auer rods indicate acute myelogenous leukemia. Patients typically develop complications of pancytopenia, including fatigue (anemia), fever due to infection (neutropenia), and ecchymosis or epistaxis (thrombocytopenia).

**(Choice C)** Mixed cryoglobulinemia is a small- to medium-vessel vasculitis caused by circulating immunoglobulin-complement complexes that precipitate on refrigeration. It is typically associated with chronic inflammatory states (eg, systemic lupus erythematosus, hepatitis C) and can present with systemic findings (eg, fatigue, arthralgias, myalgias) and palpable purpura in the lower extremities due to cutaneous vasculitis.

**(Choice E)** Microangiopathic hemolytic anemia usually presents with anemia and fragmented red blood cells (schistocytes) on the peripheral smear. It has been associated with cancer chemotherapy drugs (eg, cisplatin, cyclophosphamide).

**Educational objective:**
Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome typically occurs 2-8 weeks after exposure to high-risk drugs such as anticonvulsants (eg, phenytoin, carbamazepine), allopurinol, sulfonamides (eg, sulfasalazine), and antibiotics (eg, minocycline, vancomycin). Patients typically develop fever, generalized lymphadenopathy, facial edema, diffuse skin rash, eosinophilia, and internal organ


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**(Choice C)** Mixed cryoglobulinemia is a small- to medium-vessel vasculitis caused by circulating immunoglobulin-complement complexes that precipitate on refrigeration. It is typically associated with chronic inflammatory states (eg, systemic lupus erythematosus, hepatitis C) and can present with systemic findings (eg, fatigue, arthralgias, myalgias) and palpable purpura in the lower extremities due to cutaneous vasculitis.

**(Choice E)** Microangiopathic hemolytic anemia usually presents with anemia and fragmented red blood cells (schistocytes) on the peripheral smear. It has been associated with cancer chemotherapy drugs (eg, cisplatin, cyclophosphamide).

**Educational objective:**

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome typically occurs 2-8 weeks after exposure to high-risk drugs such as anticonvulsants (eg, phenytoin, carbamazepine), allopurinol, sulfonamides (eg, sulfasalazine), and antibiotics (eg, minocycline, vancomycin). Patients typically develop fever, generalized lymphadenopathy, facial edema, diffuse skin rash, eosinophilia, and internal organ dysfunction.

**References**

- Drug reaction with eosinophilia and systemic symptoms (DRESS): an original multisystem adverse drug reaction. Results from the prospective RegiSCAR study



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A 20-year-old college student comes to the office due to falling asleep at inappropriate times. He has an irresistible urge to sleep during the day, and these "naps" occur unpredictably, sometimes at the start of class or during examinations. He sleeps 6-7 hours per night and feels refreshed when he awakens. He also experiences frightening auditory hallucinations before falling asleep. He was recently in a motor vehicle collision after falling asleep at the wheel, which resulted in only a minor sprain of his wrist. He does not use tobacco, alcohol, or illicit drugs. Physical examination is unremarkable. Which of the following is the best treatment for this patient's condition?

A. Carbamazepine
B. Clonazepam
C. Melatonin
D. Modafinil
E. Zolpidem

Submit



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A 20-year-old college student comes to the office due to falling asleep at inappropriate times. He has an irresistible urge to sleep during the day, and these "naps" occur unpredictably, sometimes at the start of class or during examinations. He sleeps 6-7 hours per night and feels refreshed when he awakens. He also experiences frightening auditory hallucinations before falling asleep. He was recently in a motor vehicle collision after falling asleep at the wheel, which resulted in only a minor sprain of his wrist. He does not use tobacco, alcohol, or illicit drugs. Physical examination is unremarkable. Which of the following is the best treatment for this patient's condition?

- A. Carbamazepine (6%)
- B. Clonazepam (5%)
- ✗ C. Melatonin (6%)
- ✓ D. Modafinil (74%)
- E. Zolpidem (7%)

Incorrect

74%  02 mins, 31 secs  01/14/2021



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| Narcolepsy | |
|---|---|
| **DSM-5 diagnostic criteria** | • Recurrent lapses into sleep or naps (≥3 times/week for 3 months)<br>• ≥1 of the following:<br>◦ Cataplexy: Brief loss of muscle tone precipitated by strong emotion (eg, laughter, excitement)<br>◦ Low cerebrospinal fluid levels of hypocretin-1<br>◦ Shortened REM sleep latency |
| **Associated features** | • Hypnagogic or hypnopompic hallucinations<br>• Sleep paralysis |

**Narcolepsy** is a rare neurologic disorder characterized by episodes of irresistible sleep during the day and usually one or more REM sleep–related phenomena such as **cataplexy** (ie, sudden weakness triggered by strong emotions), **hypnagogic/hypnopompic hallucinations** (ie, hallucinations while falling asleep or awakening, respectively), and **sleep paralysis** (ie, physiologic sleep paralysis that persists on awakening/falling asleep). The etiology of narcolepsy is believed to be due to low levels of the stimulatory neurotransmitter orexin (ie, hypocretin), which is involved in maintaining wakefulness and suppressing


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awakening, respectively), and **sleep paralysis** (ie, physiologic sleep paralysis that persists on awakening/falling asleep). The etiology of narcolepsy is believed to be due to low levels of the stimulatory neurotransmitter orexin (ie, hypocretin), which is involved in maintaining wakefulness and suppressing REM sleep–related phenomena.

Treatment involves the use of agents that promote wakefulness (psychostimulants). **Modafinil**, a nonamphetamine stimulant, has become the first-line agent because it is effective and well tolerated and its misuse is rare. The mechanism of action is not well described, but modafinil may enhance dopaminergic signaling. Amphetamines are second-line agents due to their sympathomimetic side effects (eg, hypertension, arrhythmia, psychosis) and risk for misuse and dependency.

**(Choice A)** Carbamazepine is used to treat seizures, bipolar disorder, and trigeminal neuralgia, not narcolepsy.

**(Choices B and E)** Zolpidem is a nonbenzodiazepine hypnotic used for insomnia. The use of zolpidem or a benzodiazepine (eg, clonazepam) in patients with narcolepsy is relatively contraindicated due to the risk of worsening daytime sedation.

**(Choice C)** Melatonin is used for treating jet lag and delayed sleep-wake phase syndrome, not narcolepsy.

**Educational objective:**


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misuse is rare. The mechanism of action is not well described, but modafinil may enhance dopaminergic signaling. Amphetamines are second-line agents due to their sympathomimetic side effects (eg, hypertension, arrhythmia, psychosis) and risk for misuse and dependency.

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**(Choice C)** Melatonin is used for treating jet lag and delayed sleep-wake phase syndrome, not narcolepsy.

**Educational objective:**
Treatment for narcolepsy includes psychostimulants (eg, modafinil) for daytime sleepiness.

**References**

- Treatment options for narcolepsy.
- Management of narcolepsy.


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A 6-month-old boy is evaluated in the clinic due to delayed motor development. The mother reports that the boy is weaker than other children his age. He can barely lift his head up when prone and is unable to roll to the side. Physical examination shows generalized hypotonia and decreased deep tendon reflexes. Further evaluation reveals mutation of a protein involved in the assembly of small nuclear ribonucleoproteins (snRNPs) in motor neurons. This patient most likely has impaired function of which of the following cellular elements?

A. Nucleosomes
B. Peroxisomes
C. Proteasomes
D. Ribosomes
E. Spliceosomes

Submit



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A 6-month-old boy is evaluated in the clinic due to delayed motor development. The mother reports that the boy is weaker than other children his age. He can barely lift his head up when prone and is unable to roll to the side. Physical examination shows generalized hypotonia and decreased deep tendon reflexes. Further evaluation reveals mutation of a protein involved in the assembly of small nuclear ribonucleoproteins (snRNPs) in motor neurons. This patient most likely has impaired function of which of the following cellular elements?

A. Nucleosomes (5%)
B. Peroxisomes (3%)
C. Proteasomes (4%)
D. Ribosomes (11%)
E. Spliceosomes (75%)

Correct

75% Answered correctly
44 secs Time Spent
01/31/2021 Last Updated



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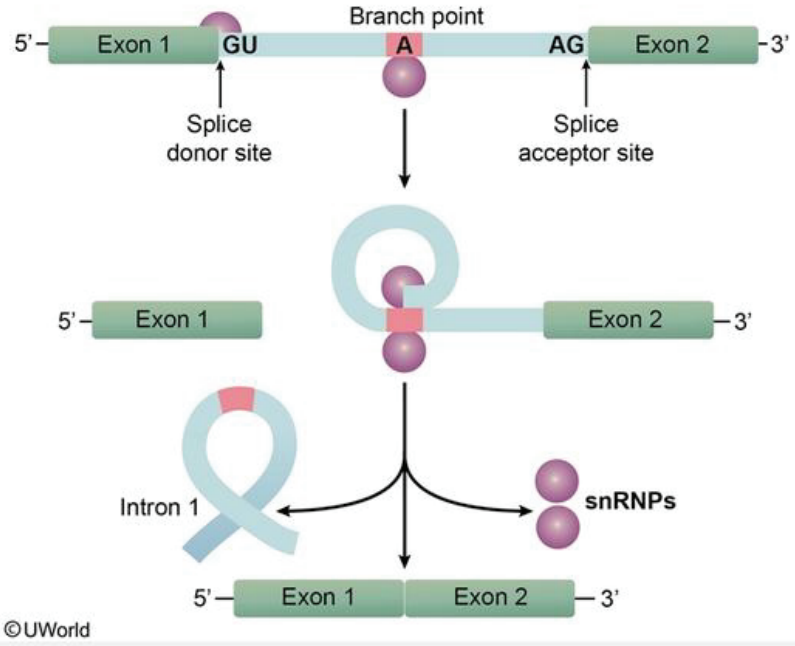
## Splicing of pre-mRNA

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This infant with delayed motor development and flaccid paralysis (eg, hypotonia, decreased deep tendon reflexes) likely has **spinal muscular atrophy**. This condition is caused by mutations in the **survival motor neuron (*SMN1*) gene**, which encodes a protein involved in assembly of **small nuclear ribonucleoproteins (snRNPs)** in lower motor neurons. Defective snRNP assembly results in impaired spliceosome function and degeneration of anterior horn cells in the spinal cord.

RNA molecules that carry out functions without first being translated into proteins are called non-coding RNAs. These include small nuclear RNA (snRNA), ribosomal RNA (rRNA), and transfer RNA (tRNA). snRNA is transcribed by RNA polymerase II and associates with specific proteins to form snRNPs. A collection of snRNPs and other proteins on pre-mRNA is referred to as a **spliceosome**. Spliceosomes **remove introns** from pre-mRNA by cleaving the 5' end of intron 1 (splice donor site) and joining that end to the branch point. The freed 3'-OH of exon 1 then forms a phosphodiester bond with the 5'-phosphate at the splice acceptor site, joining exons 1 and 2.

**(Choice A)** Eukaryotic chromatin is composed of repeated subunits called nucleosomes, which consist of double-stranded DNA wrapped around histone protein cores. Nucleosomes are important for the compact packaging of DNA into chromosomes with the aid of other packaging proteins.



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**(Choice B)** Peroxisomes are cytoplasmic organelles containing oxidative enzymes (eg, catalase, D-amino acid oxidase, uric acid oxidase). These organelles are ubiquitous among eukaryotes and are most abundant in the liver and kidneys, where detoxification of ingested and environmental materials occurs. In the liver, peroxisomes also play a role in the breakdown of fatty acids.

**(Choice C)** Proteasomes and lysosomes are responsible for protein/polypeptide degradation. Proteasomes mainly degrade intracellular proteins, whereas lysosomes degrade extracellular proteins and worn-out organelles.

**(Choice D)** Ribosomes are present in the cytoplasm and are required for translation of mRNA into protein. Individual ribosomes are comprised of rRNA and ribosomal proteins. Within the cell, rRNA engages mRNA and facilitates tRNA entry during the formation of polypeptide chains.

**Educational objective:**
Small nuclear ribonucleoproteins (snRNPs) are important components of the spliceosome, a molecule which removes introns from pre-mRNA during processing within the nucleus. Spinal muscular atrophy is a disorder caused by mutations in the *SMN1* gene, resulting in impaired assembly of snRNPs in lower motor neurons. Infants often have flaccid paralysis due to degeneration of anterior horn cells in the spinal cord.

**References**



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A 32-year-old woman comes to the office due to left eye pain that is accentuated by ocular movements. She also has periodic dimming of vision in the same eye. The patient has had several such episodes over the last month, most often after a hot shower or intense workout. A year ago, she had an episode of numbness and tingling in her left arm that resolved spontaneously. The patient has no other medical issues and takes no medication. She smokes half a pack of cigarettes a day and does not use alcohol or illicit drugs. Vital signs are normal. BMI is 26 kg/m$^2$. Ophthalmologic examination shows swelling of the optic disc on the left. Neurologic examination shows a mild intention tremor and broad-based gait. Which of the following is the most likely cause of the patient's current condition?

A. Atherosclerosis of the carotid arteries
B. Brain metastasis
C. Demyelinating plaques
D. Increased red blood cell mass
E. *Treponema pallidum* infection
F. Vitamin $B_{12}$ deficiency


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A. Atherosclerosis of the carotid arteries (3%)
B. Brain metastasis (1%)
C. Demyelinating plaques (81%)
D. Increased red blood cell mass (10%)
E. *Treponema pallidum* infection (1%)
F. Vitamin $B_{12}$ deficiency (1%)


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| Multiple sclerosis | |
|---|---|
| **Common presenting symptoms** | • Sensory disturbances, motor weakness, bowel/bladder dysfunction<br>• Ocular manifestations: Optic neuritis (painful eye movement), internuclear ophthalmoplegia (impaired adduction on lateral gaze)<br>• Lhermitte sign: Electrical sensation in limbs or back<br>• Uhthoff phenomenon: Symptom worsening with increased body temperature |
| **Risk factors** | • Female, Caucasian, *HLA-DRB1*<br>• Environmental factors: Location (USA, Europe), cold climate<br>• Low vitamin D levels<br>• Smoking |
| **Diagnosis** | • Episodic/progressive symptoms disseminated over time & space<br>• Hyperintense lesions on T2-weighted MRI<br>• Oligoclonal IgG bands on cerebrospinal fluid analysis |

This patient has eye pain worsened with movement, intermittently decreased vision, and swelling of the optic disc, consistent with **optic neuritis**. In a young female patient, optic neuritis should raise concern for


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This patient has eye pain worsened with movement, intermittently decreased vision, and swelling of the optic disc, consistent with **optic neuritis**. In a young female patient, optic neuritis should raise concern for **multiple sclerosis** (MS), a chronic immune-mediated disease that affects the central nervous system (CNS) and leads to oligodendrocyte destruction. Demyelinating plaques are commonly seen as hyperintense lesions on T2- weighted MRI of the brain and spinal cord.

MS is characterized by episodic, progressive neurologic deficits that may involve multiple anatomic regions within the CNS (ie, **separated in space and time**). In addition to optic neuritis, other manifestations of MS include sensory/motor symptoms (eg, arm numbness and tingling), internuclear ophthalmoplegia, cerebellar dysfunction (eg, intention tremor, broad-based gait), fatigue, and Lhermitte sign (electrical sensations down the back/limbs with neck flexion). Symptom worsening can occur with increased body temperature (eg, exercise, bathing) due to slowing of neuronal conduction in unmyelinated nerves (Uhthoff phenomenon).

**(Choice A)** Atherosclerosis of the carotid arteries can cause transient ischemia leading to episodic vision loss (amaurosis fugax). However, it would not typically cause eye pain or worsening symptoms with body heat, and would be rare in a young patient without other signs of atherosclerosis.


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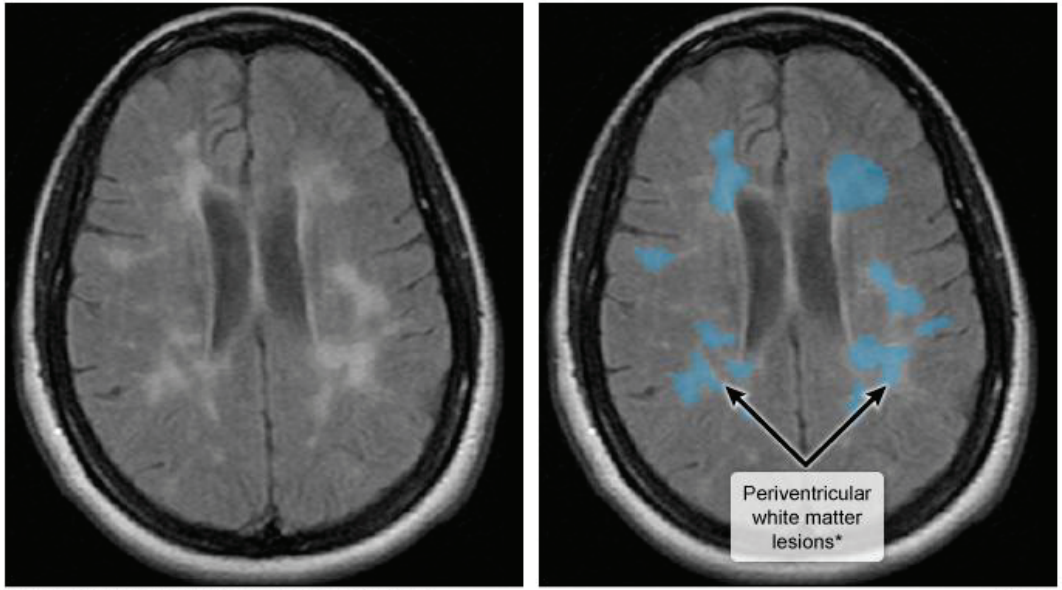
## Multiple sclerosis




*Demyelinating plaques with inflammation and gliosis

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**(Choice B)** Brain metastases can cause a variety of neurologic symptoms (eg, cerebellar signs, vision changes) but would be expected to worsen with time, not relapse and remit.

**(Choice D)** Polycythemia vera can cause transient visual disturbances and other neurologic manifestations due to increased blood viscosity. Although patients may have pruritus or erythema following heat exposure, heat does not worsen neurologic symptoms. Also, this patient does not have other polycythemic manifestations (eg, hypertension, facial plethora).

**(Choice E)** Neurosyphilis can cause a wide-based gait and pupillary irregularities (Argyll Robertson pupil; ie, accommodates but does not react to light), but there is no pain with eye movement or vision loss. In addition, heat sensitivity and upper extremity weakness would be unexpected.

**(Choice F)** Vitamin $B_{12}$ deficiency causes subacute combined degeneration, and patients can develop a broad-based gait. However, in most cases this is slowly progressive and often accompanied by paresthesias in the distal lower extremities. Intention tremor and optic neuritis are not associated with vitamin $B_{12}$ deficiency.

**Educational objective:**

Multiple sclerosis is characterized by episodic, progressive neurologic deficits involving multiple anatomic regions within the central nervous system. Demyelinating plaques are commonly seen as hyperintense


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heat exposure, heat does not worsen neurologic symptoms. Also, this patient does not have other polycythemic manifestations (eg, hypertension, facial plethora).

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**(Choice F)** Vitamin $B_{12}$ deficiency causes subacute combined degeneration, and patients can develop a broad-based gait. However, in most cases this is slowly progressive and often accompanied by paresthesias in the distal lower extremities. Intention tremor and optic neuritis are not associated with vitamin $B_{12}$ deficiency.

**Educational objective:**
Multiple sclerosis is characterized by episodic, progressive neurologic deficits involving multiple anatomic regions within the central nervous system. Demyelinating plaques are commonly seen as hyperintense lesions on T2-weighted MRI of the brain and spinal cord. Common manifestations include optic neuritis, internuclear ophthalmoplegia, sensory deficits, and fatigue, which may worsen with heat exposure.

**References**



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A 53-year-old man comes to the office due to double vision. The patient lives in a two-story house and has had difficulty walking down stairs because he sees duplicates of every step and doesn't "know which ones are real." He does not have significant problems walking up stairs. The patient is also frustrated because he has trouble reading certain things, such as the morning newspaper and work-related documents. He has had no eye trauma, headache, focal weakness, or numbness. The patient has a history of hypertension and type 2 diabetes mellitus. He exercises regularly and does not use tobacco, alcohol, or illicit drugs. A lesion affecting which of the following structures is most likely responsible for this patient's visual symptoms?

A. Abducens nerve
B. Medial longitudinal fasciculus
C. Oculomotor nerve
D. Optic nerve
E. Trochlear nerve



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had difficulty walking down stairs because he sees duplicates of every step and doesn't "know which ones are real." He does not have significant problems walking up stairs. The patient is also frustrated because he has trouble reading certain things, such as the morning newspaper and work-related documents. He has had no eye trauma, headache, focal weakness, or numbness. The patient has a history of hypertension and type 2 diabetes mellitus. He exercises regularly and does not use tobacco, alcohol, or illicit drugs. A lesion affecting which of the following structures is most likely responsible for this patient's visual symptoms?

A. Abducens nerve (7%)
B. Medial longitudinal fasciculus (10%)
C. Oculomotor nerve (20%)
D. Optic nerve (6%)
E. Trochlear nerve (54%)

Correct

54%
54 secs
12/21/2020



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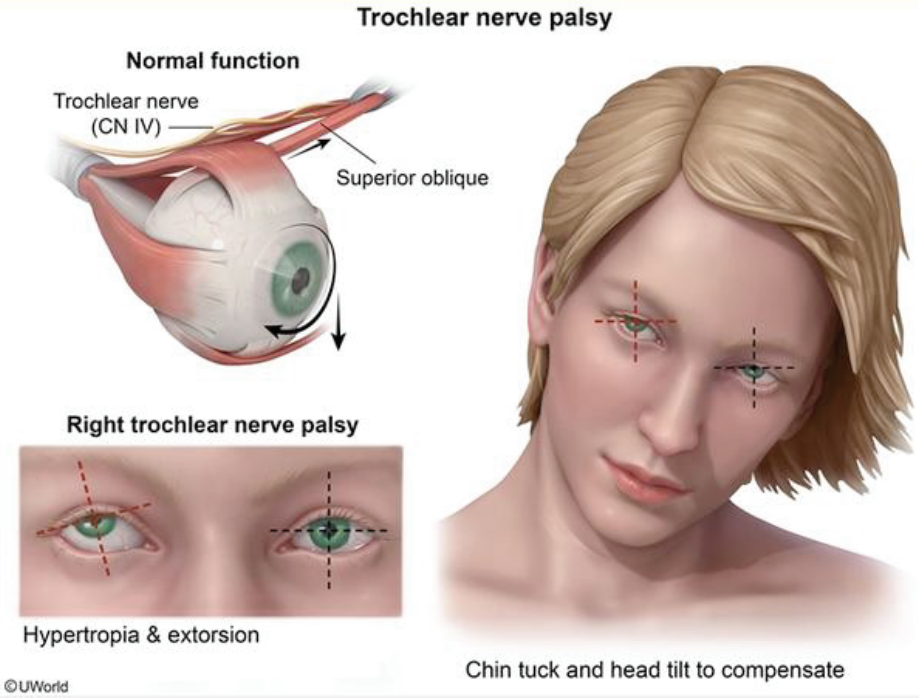


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This patient likely has **trochlear nerve (CN IV) palsy**. The trochlear nerve innervates the superior oblique muscle, which causes the eye to **intort** (internally rotate) and **depress while adducted**. The nerve is particularly susceptible to injury due to its long course and small caliber. Most cases of neuropathy are traumatic or idiopathic in origin, although a proportion of idiopathic cases may actually be due to microvascular nerve ischemia in the setting of diabetes mellitus. Patients with trochlear nerve palsy typically present with **vertical diplopia**, which is most noticeable when the affected eye looks down and toward the nose (eg, up-close reading, **walking down stairs**). Examination may show impairment of downgaze with the eye in the adducted position. In severe cases, the affected eye can appear vertically deviated (hypertropia). Symptoms often improve when the chin is tucked and the head is tilted away from the affected eye as this compensates for hypertropia and extorsion.

**(Choice A)** The abducens nerve (cranial nerve [CN] VI) innervates the lateral rectus, which is responsible for abduction of the eye. Palsies of this nerve can cause horizontal diplopia and inward deviation (esotropia).

**(Choice B)** Lesions of the medial longitudinal fasciculus are associated with internuclear ophthalmoplegia. This typically presents with impaired horizontal eye movement and weak adduction of the affected eye with simultaneous abduction nystagmus of the contralateral eye.



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**(Choice A)** The ab
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**(Choice B)** Lesion
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| Nerve | Eye muscle(s) innervated | Oculomotor functions | Lesion findings |
|---|---|---|---|
| **Oculomotor (CN III)** | • Superior rectus<br>• Medial rectus<br>• Inferior rectus<br>• Inferior oblique<br>• Levator palpebrae superioris | • Adduction<br>• Depression<br>• Elevation<br>• External rotation | • Eye deviated downward & laterally<br>• Diagonal diplopia<br>• Dilation of pupil & loss of accommodation<br>• Ptosis |
| **Trochlear (CN IV)** | • Superior oblique | • Abduction<br>• Internal rotation<br>• Depression while adducted | • Eye deviated upward<br>• Vertical & torsional diplopia |
| **Abducens (CN VI)** | • Lateral rectus | • Abduction | • Eye deviated medially<br>• Horizontal diplopia |

New | Existing



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**(Choice B)** Lesions of the medial longitudinal fasciculus are associated with internuclear ophthalmoplegia. This typically presents with impaired horizontal eye movement and weak adduction of the affected eye with simultaneous abduction nystagmus of the contralateral eye.

**(Choice C)** The oculomotor nerve (CN III) innervates the superior rectus, medial rectus, inferior rectus, and inferior oblique. These muscles collectively perform most eye movements. Palsies of this nerve can cause vertical and horizontal diplopia, ptosis, and an enlarged and nonreactive pupil.

**(Choice D)** The optic nerve (CN II) transmits visual information to the brain. Damage to this nerve causes loss of vision.

**Educational objective:**

The trochlear nerve innervates the superior oblique muscle, which causes the eye to intort (internally rotate) and depress while adducted. Trochlear nerve palsy is typically traumatic or idiopathic and presents with vertical diplopia that worsens when the affected eye looks down and toward the nose (eg, walking downstairs, up-close reading). Patients may compensate by tucking the chin and tilting the head away from the affected eye.

**References**

- Adult hypertropia: a guide to diagnostic evaluation based on review of 300 patients.



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A 44-year-old woman comes to the office for follow-up. The patient sustained a complete C7 spinal cord injury a year ago after falling off a cliff while hiking. She is able to move her shoulders and upper arms but has paraplegia and uses a wheelchair. The patient has a suprapubic catheter due to neurogenic bladder. She has no other medical conditions. She is a lifelong nonsmoker. Which of the following changes in respiratory parameters are most likely present in this patient?

| | Maximal inspiratory pressure | Maximal expiratory pressure |
|---|---|---|
| A. | Decreased | Increased |
| B. | Decreased | Normal |
| C. | Normal | Decreased |
| D. | Increased | Decreased |
| E. | Increased | Increased |


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injury a year ago after falling off a cliff while hiking. She is able to move her shoulders and upper arms but has paraplegia and uses a wheelchair. The patient has a suprapubic catheter due to neurogenic bladder. She has no other medical conditions. She is a lifelong nonsmoker. Which of the following changes in respiratory parameters are most likely present in this patient?

| | Maximal inspiratory pressure | Maximal expiratory pressure | |
|---|---|---|---|
| A. | Decreased | Increased | (6%) |
| B. | Decreased | Normal | (36%) |
| C. | Normal | Decreased | (50%) |
| D. | Increased | Decreased | (5%) |
| E. | Increased | Increased | (1%) |

Correct

50%

39 secs

11/25/2020



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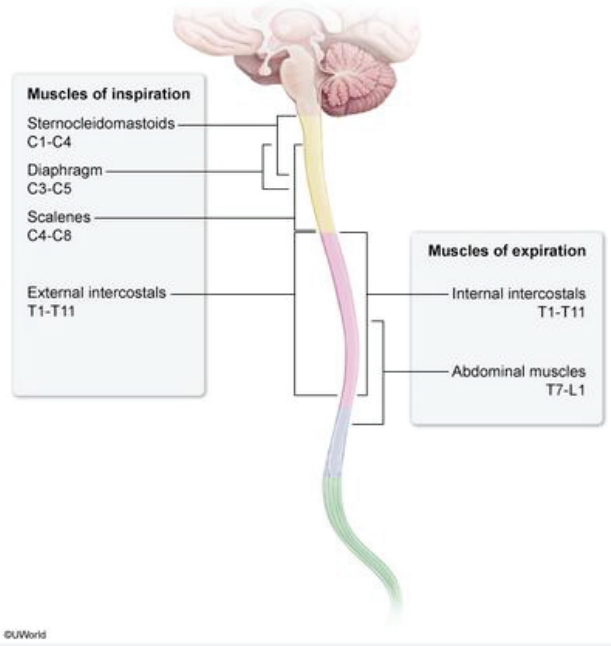
Respiratory muscle innervation

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Patients with **spinal cord injuries** often have significant alterations in **respiratory dynamics**. Because different muscles (with different sources of innervation) control inspiration and expiration, respiratory function is differentially impaired based on the level of spinal cord injury.

**Inspiration** is driven by an increase in intrathoracic volume. This is mediated predominantly by contraction of the **diaphragm**, which is innervated by the **phrenic nerve** that originates from the **C3-C5** nerve rootlets. Accessory muscles of inspiration elevate the sternum and ribs to further expand the thoracic cavity. These include the external intercostals (innervated by thoracic nerve roots), the sternocleidomastoid (innervated by C1-C4), and the scalenes (innervated by C4-C8).

Passive expiration is driven by the net intrinsic elastic recoil of the lungs, chest wall, ribs, and diaphragm and therefore requires no innervation. **Active expiration**, as measured in this patient's pulmonary function testing, recruits the musculature to pull the ribs down and compress the abdominal contents to push the diaphragm up and decrease intrathoracic volume. This is driven by the **internal intercostals** (innervated by **thoracic nerve roots**) and **abdominal muscles** (innervated by **thoracic and lumbar nerve roots**).

Because the spinal cord injury was at the **level of C7** in this patient, the diaphragm and many of the accessory inspiratory muscles are likely functional, resulting in minimal impairment of maximal inspiratory



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by **thoracic nerve roots**) and **abdominal muscles** (innervated by **thoracic and lumbar nerve roots**).

Because the spinal cord injury was at the **level of C7** in this patient, the diaphragm and many of the accessory inspiratory muscles are likely functional, resulting in minimal impairment of maximal inspiratory pressure. However, the muscles involved in active expiration (ie, internal intercostals and abdominal muscles) are likely significantly impaired, leading to a significant **decrease in maximal expiratory pressure**.

**(Choices A and B)** Although the external intercostals are innervated by thoracic nerve roots and may be impaired in this patient, the other accessory muscles of inspiration, including the sternocleidomastoid and scalenes, are typically able to compensate for their loss and adequately elevate the sternum/ribs. This leads to minimal or no change in the maximal inspiratory pressure.

**Educational objective:**
The diaphragm is the principal muscle of inspiration and is innervated by the phrenic nerve, which originates from the C3-5 nerve rootlets. Although expiration is largely achieved through passive recoil, active expiration is aided by the internal intercostals (innervated by thoracic nerve rootlets) and abdominal muscles (innervated by thoracic and lumbar nerve roots).

Physiology Nervous System Spinal cord injury


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A 30-year-old man with a history of epilepsy comes to the office for follow-up. He has a history of recurrent seizures that start as jerky, rhythmic movements of his left leg and gradually spread to involve the entire left side of his body. The patient frequently loses consciousness and has been witnessed to have a generalized tonic-clonic seizure. Neuroimaging has revealed a focal lesion in the right motor area. He has been treated with several antiepilepsy drugs, but his seizures have remained poorly controlled. Surgery is performed to remove the lesion, and the excised brain tissue shows a 1.5-cm mass composed of engorged purplish clusters. Microscopy shows numerous dilated capillaries with an endothelial lining separated by a thin layer of fibrous connective tissue. Which of the following is the most likely diagnosis?

- A. Cavernous hemangioma
- B. Ependymoma
- C. Glioblastoma
- D. Kaposi sarcoma
- E. Saccular aneurysm



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seizures that start as jerky, rhythmic movements of his left leg and gradually spread to involve the entire left side of his body. The patient frequently loses consciousness and has been witnessed to have a generalized tonic-clonic seizure. Neuroimaging has revealed a focal lesion in the right motor area. He has been treated with several antiepilepsy drugs, but his seizures have remained poorly controlled. Surgery is performed to remove the lesion, and the excised brain tissue shows a 1.5-cm mass composed of engorged purplish clusters. Microscopy shows numerous dilated capillaries with an endothelial lining separated by a thin layer of fibrous connective tissue. Which of the following is the most likely diagnosis?

- A. Cavernous hemangioma (76%)
- B. Ependymoma (6%)
- C. Glioblastoma (7%)
- D. Kaposi sarcoma (5%)
- E. Saccular aneurysm (3%)

Correct

76%

57 secs

03/04/2021



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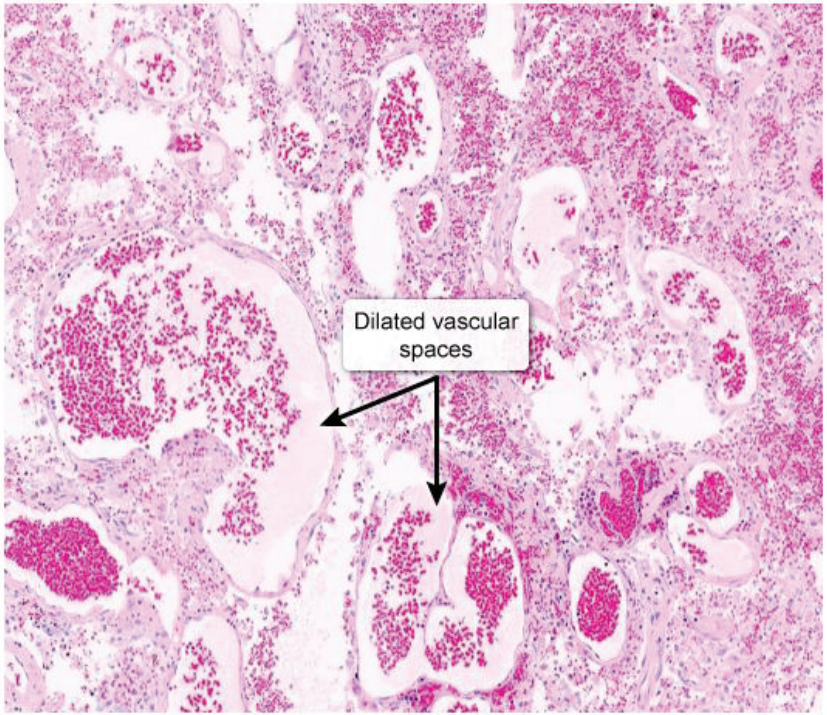
## Cerebral cavernous hemangioma



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**Cavernous hemangiomas** are vascular malformations that frequently involve the deeper tissues of the body, such as the liver and brain. Gross examination of hemangiomas reveals a "mulberry-like" appearance due to their purple vascular clusters. Histologically, they are composed of abnormal, **dilated blood vessels** with a thin adventitia lacking elastic fibers and smooth muscle. The reduced structural support gives them a tendency to leak, causing **recurrent hemorrhage**.

Most patients with cavernous hemangiomas are asymptomatic, although hemangiomas in the brain may cause **neurologic deficits** and **seizures** due to compression of the surrounding tissue and irritation from recurrent bleeding. Surgical resection is indicated for lesions causing intractable epilepsy or progressive neurologic deficits.

**(Choice B)** Ependymoma is a rare central nervous system tumor typically found intracranially in children and in the spinal cord in adults. The tumor cells may arrange themselves around blood vessels and form intervening processes, a histological appearance called perivascular pseudorosettes.

**(Choice C)** Glioblastoma is a common and aggressive brain tumor characterized histologically by areas of necrosis surrounded by tumor cells (pseudopalisading necrosis).

**(Choice D)** Kaposi sarcoma is a tumor that results from infection with human herpesvirus 8. It typically



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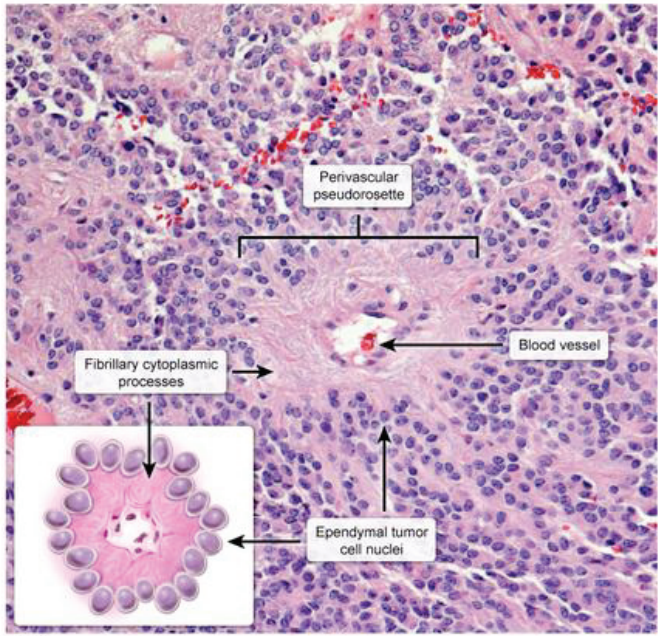
Ependymoma

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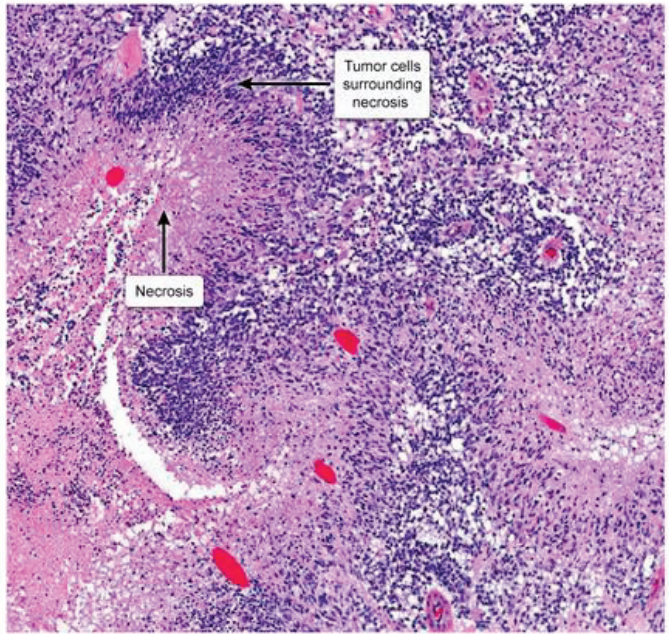
Glioblastoma

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necrosis surrounded by tumor cells (pseudopalisading necrosis).

**(Choice D)** Kaposi sarcoma is a tumor that results from infection with human herpesvirus 8. It typically manifests as skin nodules but can also affect the gastrointestinal and respiratory tracts. Microscopic evaluation reveals highly vascular tissue containing elongated spindle cells.

**(Choice E)** Saccular (berry) aneurysms are vascular outpouchings composed of a thickened intima due to myointimal hyperplasia with a stretched adventitial layer. They occur as a result of congenital blood vessel weakness and are found most commonly in the circle of Willis. Intracranial aneurysms are typically asymptomatic unless they rupture.

**Educational objective:**
Cavernous hemangiomas are vascular malformations composed of abnormally dilated capillaries separated by thin connective tissue septa. The lack of structural support gives them a tendency to bleed, and those that occur in the brain can present with neurologic deficits and seizures.

| Pathology | Nervous System | Hemangioma |
|---|---|---|
| Subject | System | Topic |

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(Choice C) Glioblastoma is a common and aggressive brain tumor characterized histologically by areas of

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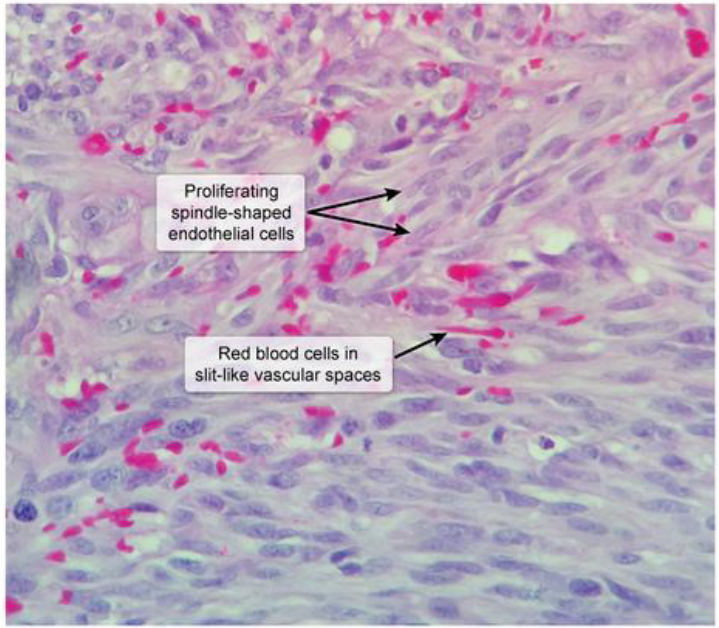
Kaposi sarcoma

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A 34-year-old woman with sleep problems comes to the office. Over the last year, she has had increasing difficulty falling asleep at night and is exhausted during the day. The patient does not use alcohol, tobacco, or illicit drugs. She has a family history of heart disease and depression. The patient has failed a number of nonpharmacological approaches, including cognitive-behavioral therapy for insomnia. She requests pharmacologic treatment and is prescribed a short course of zolpidem. Which of the following is the most likely mechanism of action of this medication?

A. Dopamine receptor antagonism
B. GABA receptor agonism
C. Histamine receptor antagonism
D. Melatonin receptor agonism
E. Orexin receptor antagonism
F. Serotonin receptor agonism

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A. ~~Dopamine receptor antagonism~~ (1%)
✓ B. GABA receptor agonism (74%)
C. ~~Histamine receptor antagonism~~ (1%)
D. ~~Melatonin receptor agonism~~ (13%)
E. Orexin receptor antagonism (6%)
F. ~~Serotonin receptor agonism~~ (2%)


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**Zolpidem** is a short-acting **nonbenzodiazepine** hypnotic agent. Other medications in this class include zaleplon and eszopiclone. Like benzodiazepines, these medications bind to the $GABA_A$ receptor at the benzodiazepine receptor site, where they act as **$GABA_A$ agonists**. However, they are chemically distinct from benzodiazepines, and their binding is more specific for certain receptor subtypes. As a result, nonbenzodiazepines are primarily **hypnotics** and do not produce the anxiolytic, muscle relaxant, or anticonvulsant effects associated with benzodiazepines.

Nonbenzodiazepines cause similar side effects to benzodiazepines (eg, next-day somnolence, cognitive dysfunction, increased risk of falls in older adults). They should be used for the shortest time possible and at the lowest effective dose.

**(Choice A)** Dopamine receptor antagonism is the mechanism of action of antipsychotic medication (eg, haloperidol, risperidone).

**(Choice C)** Histamine receptor antagonism is the mechanism of action of antihistamines (eg, diphenhydramine). Although antihistamines are often used as over-the-counter sleep aids, there is little evidence for benefit in insomnia.

**(Choice D)** Melatonin receptor agonism is the mechanism of action of the insomnia medication ramelteon


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haloperidol, risperidone).

**(Choice C)** Histamine receptor antagonism is the mechanism of action of antihistamines (eg, diphenhydramine). Although antihistamines are often used as over-the-counter sleep aids, there is little evidence for benefit in insomnia.

**(Choice D)** Melatonin receptor agonism is the mechanism of action of the insomnia medication ramelteon.

**(Choice E)** Orexin receptor antagonism is the mechanism of action of the insomnia medication suvorexant.

**(Choice F)** Serotonin receptor agonism is the mechanism of action of triptans used to treat migraine headaches and of psychedelics (eg, psilocybin, LSD).

**Educational objective:**

Nonbenzodiazepine medications (eg, zolpidem, zaleplon, eszopiclone) stimulate specific subtypes of $GABA_A$ receptors. As a result, nonbenzodiazepines are primarily hypnotics and do not produce the anxiolytic, muscle relaxant, or anticonvulsant effects associated with benzodiazepines.

**References**

- Randomised clinical trial of the effects of prolonged-release melatonin, temazepam and zolpidem on slow-wave activity during sleep in healthy people



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www.ncbi.nlm.nih.gov/pubmed/25922426

A 62-year-old man comes to the office for follow-up. The patient has a 10-year history of type 2 diabetes mellitus. Over the past 2 years, he has had burning pain and pins and needle sensations in his feet, which is worse at nighttime. Nortriptyline was prescribed, and the dosage was gradually increased. Currently, the patient takes the maximal recommended dose but states the symptoms are not well controlled. He reports no drug adverse effects. Other medical history includes hypertension and hyperlipidemia. Blood pressure is 124/70 mm Hg and pulse is 68/min. Physical examination shows decreased light touch and pain sensation in the feet. Ankle reflexes are decreased bilaterally. His most recent hemoglobin A1c level is 7.0%. Appropriate foot care is advised, and additional pharmacotherapy for the patient's symptoms is planned. Which of the following medications would provide additional benefit through a different mechanism with no drug-drug interaction?

A. Amitriptyline
B. Desipramine
C. Duloxetine
D. Gabapentin
E. Venlafaxine


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A. ~~Amitriptyline~~ (2%)

B. Desipramine (2%)

C. Duloxetine (9%)

D. Gabapentin (81%)

E. ~~Venlafaxine~~ (5%)

Incorrect
Correct answer

81%

02 mins, 21 secs

02/03/2021



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| Drugs for neuropathic pain | |
|---|---|
| **Drug** | **Mechanism of action** |
| Tricyclic antidepressants (eg, amitriptyline, nortriptyline)<br><br>SNRIs (eg, duloxetine) | • ↓ Reuptake of serotonin & norepinephrine<br>• Inhibition of pain signals |
| Anticonvulsants (eg, gabapentin, pregabalin) | • Decreased depolarization of neurons in CNS |
| Opioids | • Activation of central opioid receptors |
| Capsaicin (topical) | • Loss of membrane potential in nociceptive fibers |
| Lidocaine (topical) | • Decreased depolarization of neurons in peripheral nerves |

**CNS** = central nervous system; **SNRIs** = serotonin-norepinephrine reuptake inhibitors.

First-line therapy for painful diabetic neuropathy includes the following three classes of medications:


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**CNS** = central nervous system; **SNRIs** = serotonin-norepinephrine reuptake inhibitors.

First-line therapy for painful diabetic neuropathy includes the following three classes of medications:

- **Tricyclic antidepressants** (TCAs) (eg, nortriptyline, amitriptyline) modulate pain transmission by inhibiting voltage-gated sodium channels in sensory nerves and **increasing norepinephrine** signaling in the central nervous system (CNS).
- **Serotonin-norepinephrine reuptake inhibitors** (SNRIs) (eg, duloxetine, venlafaxine) alter central transmission of pain by **increasing norepinephrine** in the central synapses.
- Anticonvulsants (eg, gabapentin, pregabalin) inhibit the release of excitatory neurotransmitters by binding to voltage-gated calcium modulators on nerve terminals.

This patient is being treated with nortriptyline, a **TCA** drug. His symptoms are uncontrolled; therefore, an additional medication with a **different mechanism of action** should be added to avoid additive or potentially even synergistic adverse effects. **Gabapentin** does not inhibit serotonin and norepinephrine in the CNS but rather inhibits the release of excitatory neurotransmitters, so it is less likely to compound the adverse effects of a TCA.

**(Choices A and B)** Amitriptyline and desipramine, like nortriptyline, are both TCAs and should not be used


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potentially even synergistic adverse effects. **Gabapentin** does not inhibit serotonin and norepinephrine in the CNS but rather inhibits the release of excitatory neurotransmitters, so it is less likely to compound the adverse effects of a TCA.

**(Choices A and B)** Amitriptyline and desipramine, like nortriptyline, are both TCAs and should not be used concurrently because the combination can result in excess toxicity (eg, delirium, arrhythmias, seizures).

**(Choices C and E)** Duloxetine and venlafaxine are both SNRIs, which, like TCAs, inhibit serotonin and norepinephrine uptake in the CNS; therefore, TCAs and SNRIs are not typically used in combination.

**Educational objective:**
Pain due to diabetic neuropathy may be difficult to control and require multiple medications. To reduce the risk of adverse effects and improve pain control, medications should work through different mechanisms. One such combination may include a tricyclic antidepressant (eg, nortriptyline) and an anticonvulsant (eg, gabapentin).

| Pharmacology | Nervous System | Diabetic neuropathy |
|---|---|---|
| Subject | System | Topic |

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A 58-year-old man comes to the office due to worsening right upper extremity weakness over the past 4 weeks. The patient frequently travels for work and has had difficulty carrying heavy bags and getting luggage into or out of the overhead bins. He also has had neck and shoulder pain for the past several months, which he attributes to stress. The patient reports no trauma, and medical history is significant for hypertension. Physical examination shows weakness of shoulder abduction and loss of the biceps reflex on the right side. Pinprick sensation is decreased over the right lateral arm and forearm. Which of the following pathologic processes is most likely underlying this patient's current symptoms?

A. Axonal loss in the corticospinal tracts
B. Cystic expansion of the central canal
C. Degenerative changes in the vertebral joints
D. Microinjury and tear of the rotator cuff tendons
E. Rupture of the long head of the biceps tendon

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A. Axonal loss in the corticospinal tracts (7%)
B. Cystic expansion of the central canal (16%)
C. Degenerative changes in the vertebral joints (52%)
D. Microinjury and tear of the rotator cuff tendons (17%)
E. Rupture of the long head of the biceps tendon (5%)

Correct

52%

01 min, 22 secs

12/31/2020



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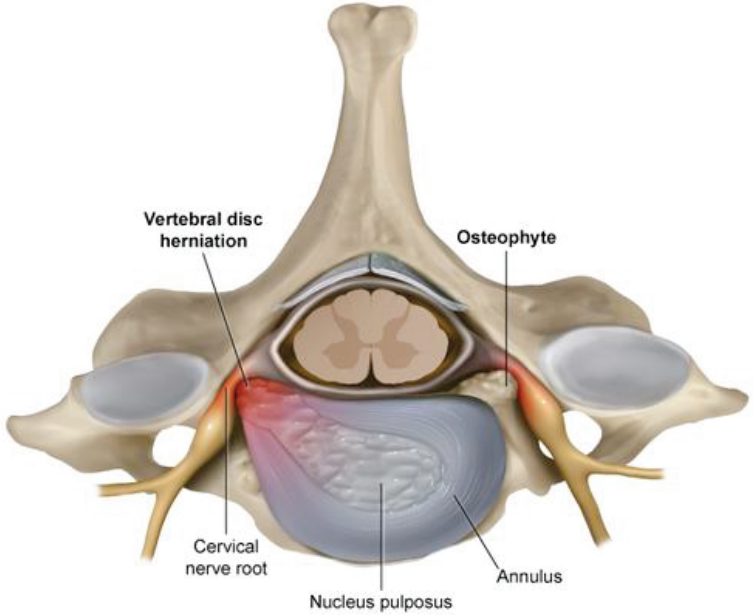
Mechanisms of radiculopathy

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This patient's sensory (eg, lateral arm/forearm sensation loss) and motor deficits (eg, impaired shoulder abduction, biceps reflex) are not isolated to the distribution of a single peripheral nerve (eg, median, ulnar), but rather follow the **C5 dermatomal and myotomal distribution**, indicating **cervical radiculopathy**.

The manifestations of cervical radiculopathies vary depending on the affected nerve root but typically present with **neck or arm pain** associated with motor and/or sensory deficits. Radiculopathies occur due to **compression of spinal nerve roots**, which is most commonly due to either:

- **Spinal spondylosis:** Aging leads to **degeneration** of the vertebral bodies, discs, and joints. Disc space decreases, and joint stress results in osteophyte (eg, bone spur) formation, which slowly narrows the neural foramina and leads to a **subacute onset** of symptoms (as seen in this patient).
- **Vertebral disc herniation:** Degeneration of ligamentous fibers can lead to a tear in the intervertebral disc annulus, resulting in herniation of the nucleus pulposus with potential nerve root compression. Disc rupture typically occurs acutely (eg, during weight lifting).

**(Choice A)** Axonal loss in the corticospinal tracts occurs in amyotrophic lateral sclerosis, a neurodegenerative disease that affects both upper and lower motor neurons. Although it can result in weakness and atrophy, it would also result in upper motor neuron signs (eg, hyperreflexia), and sensory disturbances would be atypical



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**Features of cervical radiculopathy**

| Nerve root (Disc space) | Reflex affected | Sensory loss* | Weakness |
|---|---|---|---|
| **C5** (C4-5) | • Biceps | • Lateral upper arm | • Shoulder abduction (deltoid)<br>• Elbow flexion (biceps) |
| **C6** (C5-6) | • Biceps<br>• Brachioradialis | • Thumb<br>• Index finger | • Elbow flexion (biceps)<br>• Forearm pronation/supination (brachioradialis)<br>• Wrist extension |
| **C7** (C6-7) | • Triceps | • Dorsal forearm<br>• Middle finger | • Elbow extension (triceps)<br>• Wrist flexion<br>• Finger extension |
| **C8** (C7-T1) | • Finger flexors** | • Ring & little fingers | • Finger flexion & extension<br>• Thumb flexion & abduction |
| **T1** (T1-2) | • Finger flexors** | • Medial forearm | • Finger abduction & adduction |

*In addition to neck/shoulder pain, radicular pain typically has a similar distribution to sensory loss.
**Not typically evaluated clinically.

New | Existing

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**(Choice A)** Axona
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disturbances would be atypical.

**(Choice B)** Syringomyelia results from cystic expansion of the central canal in the spinal cord. This can result in upper extremity weakness and sensory deficits, but because it expands from the central portion of the spinal cord, both upper extremities are typically affected, most often in a "cape" distribution.

**(Choice D)** Microinjury and tear of the rotator cuff tendons can result in weakness of shoulder abduction. However, sensory deficits are unexpected.

**(Choice E)** Rupture of the long head of the biceps tendon could result in shoulder pain that is aggravated by repetitive overhead activities; a loss of the biceps reflex may be observed if the rupture is complete. However, it would not cause weakness of shoulder abduction (biceps flexes and supinates the forearm) and sensory deficits would not be present.

**Educational objective:**
Cervical radiculopathy typically results in neck and/or arm pain associated with neurologic deficits that follow a dermatomal/myotomal pattern. Osteophytes that form due to degenerative changes in the vertebral joints can progressively narrow the neural foramina leading to nerve root compression.

Anatomy Nervous System Radiculopathy


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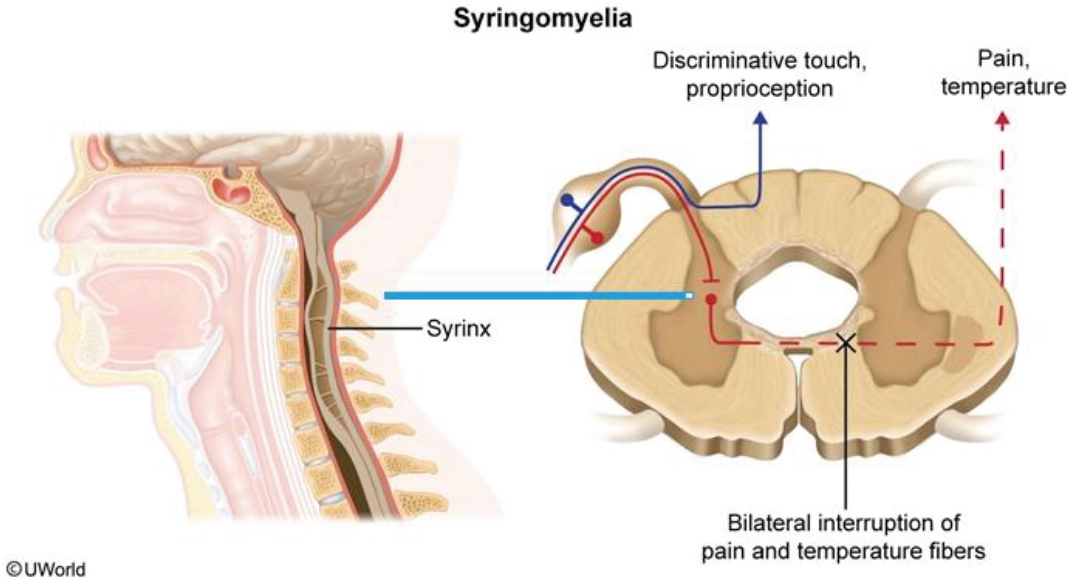


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A 62-year-old man comes to the office reporting double vision. He first noticed mild difficulty focusing his eyes about 3 weeks ago, and his symptoms have progressively worsened. The patient's other medical problems include metastatic prostate cancer. On neurologic examination, he is unable to adduct his left eye, and stimulation of the left cornea does not elicit a corneal reflex. A lesion involving which of the following anatomical structures is most likely responsible for this patient's symptoms?

- A. Foramen lacerum
- B. Foramen ovale
- C. Foramen rotundum
- D. Inferior orbital fissure
- E. Optic canal
- F. Superior orbital fissure

Submit



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- A. Foramen lacerum (1%)
- B. Foramen ovale (5%)
- C. Foramen rotundum (5%)
- D. Inferior orbital fissure (7%)
- E. Optic canal (6%)
- ✓ F. Superior orbital fissure (73%)

Correct

73% Answered correctly

59 secs Time Spent

01/18/2021 Last Updated



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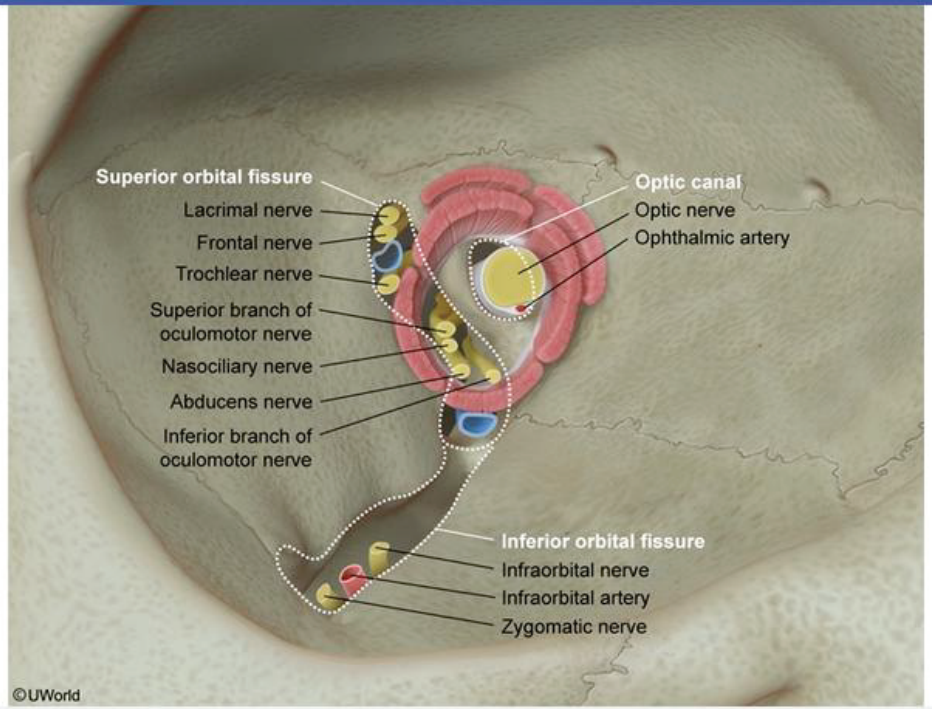


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This patient has an absence of the blink reflex on stimulation of the left cornea, indicating a lesion in the afferent limb of the reflex. In combination with a deficit of globe adduction, this suggests a lesion at the **superior orbital fissure**.

The **sensory limb of the corneal reflex** is mediated by the nasociliary branch of the first division of the trigeminal nerve (**CN $V_1$**), which enters the orbit through the superior orbital fissure. The motor component of the corneal reflex is carried primarily by the temporal branch of the facial nerve (CN VII) and causes a bilateral eye blink.

**Globe adduction** is mediated by the **medial rectus** muscle, which is innervated by the **oculomotor nerve** (CN III). The oculomotor nerve originates in the oculomotor nucleus of the midbrain, emerges from the anterior midbrain, and enters the orbit through the superior orbital fissure.

Most patients with lesions at the superior orbital fissure present with multiple deficits that may include ophthalmoplegia (oculomotor, trochlear, and abducens nerves); ptosis (levator palpebrae innervated by the oculomotor nerve); a fixed, dilated pupil (sympathetics of oculomotor nerve); and lacrimal hyposecretion and forehead numbness (V1).

**(Choice A)** The foramen lacerum is occluded by cartilage. The internal carotid artery courses just superior



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**(Choice A)** The foramen lacerum is occluded by cartilage. The internal carotid artery courses just superior to the foramen lacerum in the lacerum portion of the carotid canal.

**(Choice B)** The mandibular branch of the trigeminal nerve (CN $V_3$) passes through the foramen ovale.

**(Choice C)** The foramen rotundum transmits the maxillary division of the trigeminal nerve (CN $V_2$) from within the skull to the pterygopalatine fossa. From there, it courses through the inferior orbital fissure to appear on the face at the infraorbital foramen as the infraorbital nerve.

**(Choice D)** The maxillary division of the trigeminal nerve (CN $V_2$), the infraorbital vessels, and branches from the sphenopalatine ganglion pass through the inferior orbital fissure but do not enter the orbit.

**(Choice E)** The optic canal is medial to the superior orbital fissure and transmits the optic nerve (CN II) and ophthalmic artery.

**Educational objective:**

The oculomotor nerve (CN III), ophthalmic nerve (CN $V_1$) branches, trochlear nerve (CN IV), and abducens nerve (CN VI) enter the orbit via the superior orbital fissure.

| Anatomy | Nervous System | Cranial nerve palsy |
|---|---|---|
| Subject | System | Topic |



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(Choice A) The foramen lacerum is occluded by cartilage. The internal carotid artery courses just superior

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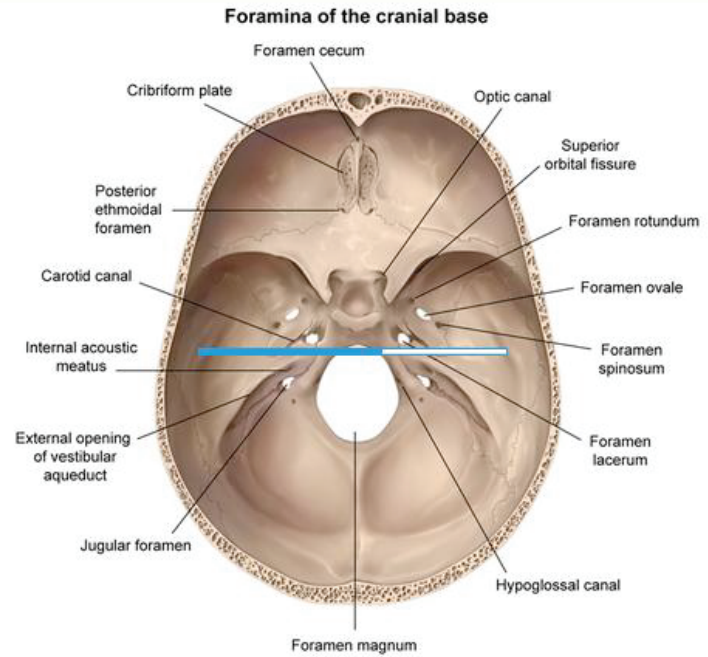


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An 82-year-old man is brought to the emergency department after multiple falls. He has had severe back pain over the last month, for which he has been taking over-the-counter pain medication without significant relief. Over the last week, the patient has noted weakness in his legs bilaterally, and his gait has become unstable. Medical history is significant for hypertension, hyperlipidemia, coronary artery disease, and gout. The patient has lost 6.8 kg (15 lb) in the last month due to poor appetite. Rectal examination reveals an enlarged, firm, nodular prostate. Which of the following is the most likely cause of this patient's current symptoms?

A. Aggregates of malignant cells in the intramedullary spinal cord
B. Compression fracture of the vertebral body
C. Extension of neoplastic cells into the epidural space
D. Intervertebral disc protrusion with spinal cord compression
E. Spondylosis resulting in spinal stenosis

Submit



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A. Aggregates of malignant cells in the intramedullary spinal cord (35%)

B. ~~Compression fracture of the vertebral body~~ (18%)

C. Extension of neoplastic cells into the epidural space (35%)

D. ~~Intervertebral disc protrusion with spinal cord compression~~ (6%)

E. ~~Spondylosis resulting in spinal stenosis~~ (4%)



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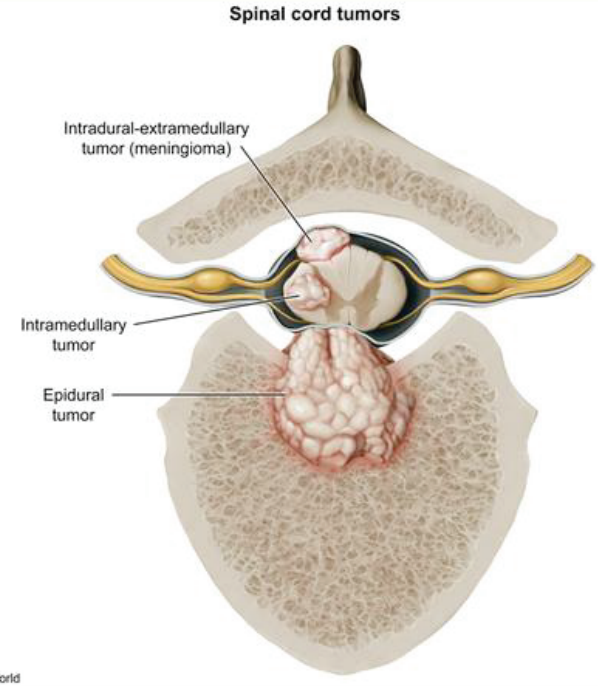


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This elderly patient with severe back pain developed lower extremity weakness and gait instability. In association with his weight loss and enlarged nodular prostate, this presentation is concerning for **neoplastic cord compression**. Spinal cord compression is a frequent complication of advanced malignancy, especially breast, lung, and prostate cancers.

Neoplastic cord compression most commonly results from **local extension of vertebral metastases** (neoplastic cells) into the **epidural space**. The tumors can encase the thecal sac and cause venous obstruction, leading to vasogenic edema, cord ischemia, and infarction. Presenting symptoms depend on the level of cord involvement but typically include **severe back pain** (often worse at night) that progresses to include **motor weakness** and/or **sensory deficits**. Urinary and fecal retention or incontinence are common late-stage findings. MRI is diagnostic.

**(Choice A)** Intramedullary metastases (malignant cells within the intramedullary spinal cord) are very rare and usually associated with lung cancer. Because of the tumor location within the spinal cord, as opposed to an adjacent structure, Brown-Séquard syndrome (ie, ipsilateral hemiplegia, contralateral sensory loss) is a common presentation.

**(Choice B)** Compression fractures are common in elderly patients, particularly those with osteoporosis, and can cause severe back pain. Although pathologic fractures can occur due to vertebral metastases


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a common presentation.

**(Choice B)** Compression fractures are common in elderly patients, particularly those with osteoporosis, and can cause severe back pain. Although pathologic fractures can occur due to vertebral metastases, subsequent cord compression due to retropulsed bone fragments occurs only rarely and is a less common cause of cord compression than direct epidural invasion by the tumor mass.

**(Choice D)** Intervertebral disc herniation can cause back pain and spinal cord compression but more commonly causes focal radiculopathy due to nerve root compression (eg, sciatica). In addition, this patient's weight loss and abnormal prostate examination are more suggestive of neoplastic cord compression.

**(Choice E)** Spondylosis (age-related degeneration of the spinal column) can cause spinal stenosis (narrowing of the spinal canal) with cord compression, typically due to osteophyte formation or thickening of the ligamentum flavum. However, symptoms are typically slowly progressive rather than of rapid onset, as seen in this patient.

**Educational objective:**
Neoplastic spinal cord compression most commonly results from local extension of vertebral metastases into the epidural space. Presenting symptoms typically include severe back pain (often worse at night),


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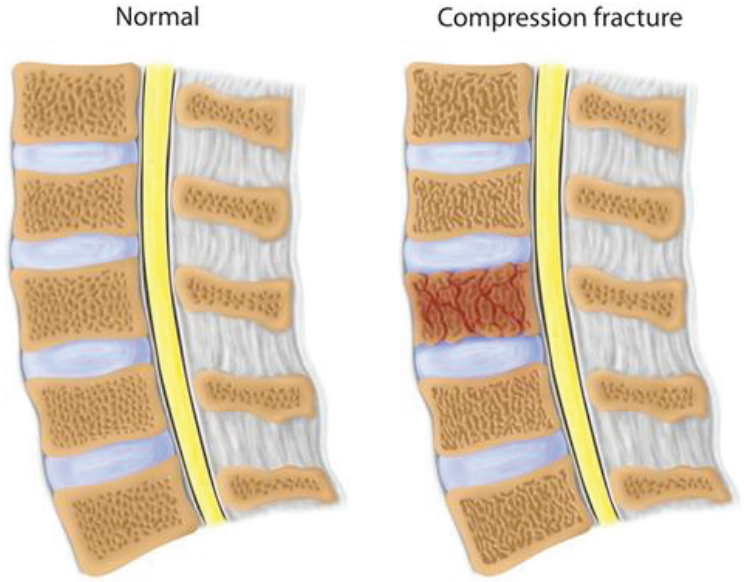
a common presentation

Exhibit Display

## Vertebral column injuries

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a common presentation

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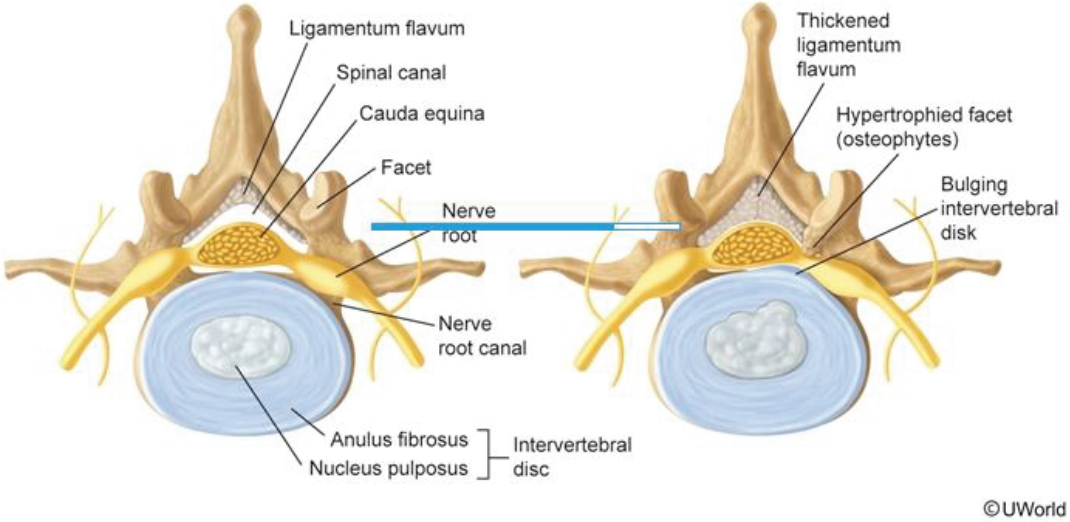


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cause of cord compression than direct epidural invasion by the tumor mass.

**(Choice D)** Intervertebral disc herniation can cause back pain and spinal cord compression but more commonly causes focal radiculopathy due to nerve root compression (eg, sciatica). In addition, this patient's weight loss and abnormal prostate examination are more suggestive of neoplastic cord compression.

**(Choice E)** Spondylosis (age-related degeneration of the spinal column) can cause spinal stenosis (narrowing of the spinal canal) with cord compression, typically due to osteophyte formation or thickening of the ligamentum flavum. However, symptoms are typically slowly progressive rather than of rapid onset, as seen in this patient.

**Educational objective:**
Neoplastic spinal cord compression most commonly results from local extension of vertebral metastases into the epidural space. Presenting symptoms typically include severe back pain (often worse at night), motor weakness, and/or sensory deficits. Urinary and fecal retention or incontinence are common late-stage findings.

| Pathology | Nervous System | Spinal cord compression |
|---|---|---|
| Subject | System | Topic |


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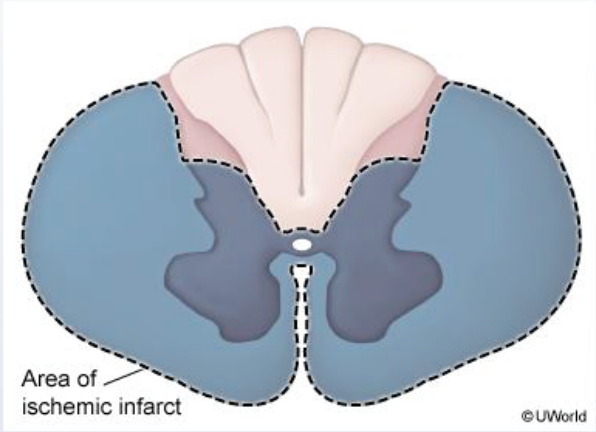
A 58-year-old man undergoes operative repair of a descending thoracic aortic aneurysm. There are no intraoperative complications, but postoperatively the patient is found to have new-onset neurologic deficits. Imaging of the brain is normal, but MRI of the lower thoracic spinal cord reveals ischemic infarct of the areas shown in the exhibit below:




Lower extremity examination of this patient is most likely to show which of the following neurologic findings?



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Lower extremity examination of this patient is most likely to show which of the following neurologic findings?

| | Crude touch | Pain sensation | Proprioception | Motor function |
|---|---|---|---|---|
| A. | ↓ | ↓ | Normal | ↓ |
| B. | ↓ | ↓ | ↓ | ↓ |
| C. | ↓ | Normal | Normal | Normal |
| D. | Normal | Normal | ↓ | ↓ |
| E. | Normal | ↓ | Normal | Normal |
| F. | Normal | Normal | ↓ | Normal |

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Lower extremity examination of this patient is most likely to show which of the following neurologic findings?

| | Crude touch | Pain sensation | Proprioception | Motor function | |
|---|---|---|---|---|---|
| ✓ A. | ↓ | ↓ | Normal | ↓ | (86%) |
| B. | ↓ | ↓ | ↓ | ↓ | (4%) |
| C. | ↓ | ~~Normal~~ | ~~Normal~~ | ~~Normal~~ | (0%) |
| D. | ~~Normal~~ | ~~Normal~~ | ↓ | ↓ | (4%) |
| E. | ~~Normal~~ | ↓ | ~~Normal~~ | ~~Normal~~ | (3%) |
| F. | ~~Normal~~ | ~~Normal~~ | ↓ | ~~Normal~~ | (0%) |

86% 01 min 01 sec 10/05/2020



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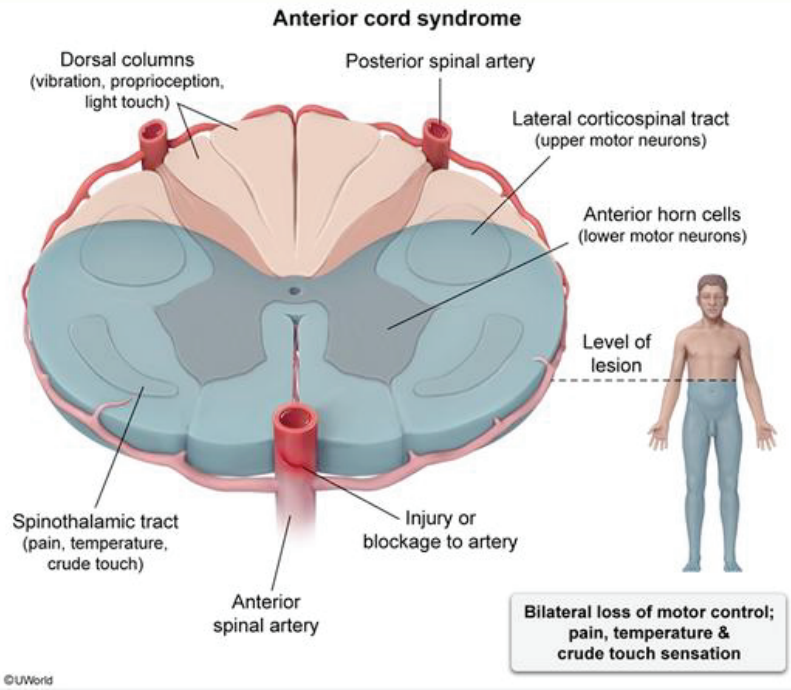


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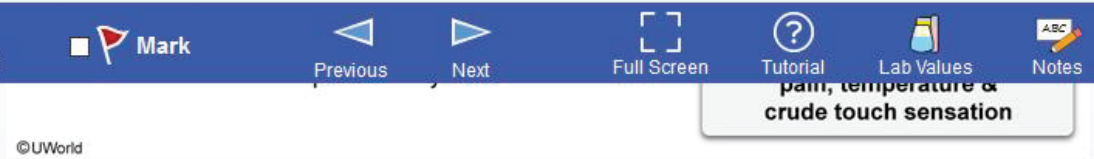


This patient's thoracic aortic aneurysm repair has been complicated by **ischemic injury** to the **anterior two-thirds** of the spinal cord (SC). This area is perfused by the **anterior spinal artery**, which receives blood flow from segmental arteries (eg, intercostal arteries) arising off the thoracic aorta. Disruption of circulation to this area classically results in **anterior cord syndrome**, characterized by the following bilateral tract lesions and clinical signs:

- Spinothalamic tract (STT): **loss** of **pain/temperature** (lateral spinothalamic) and **crude touch** (anterior spinothalamic) sensation 1-2 levels below the lesion
- Anterior horn (lower motor neuron): flaccid paralysis and muscle atrophy at the level of the lesion
- Lateral corticospinal tract (CST) (upper motor neuron): **paralysis** below the level of the lesion. Flaccid paralysis from spinal shock (ie, temporary loss of all distal SC function) occurs initially, but upper motor neuron signs (eg, spasticity, hyperreflexia) subsequently develop over days to weeks

As in this patient, the dorsal columns are typically spared (due to intact circulation from the posterior spinal arteries), preserving proprioceptive, vibratory, and light touch sensation below the level of the lesion.

**(Choice B)** Complete loss of all lower extremity sensation (due to injury of the STTs and dorsal columns)


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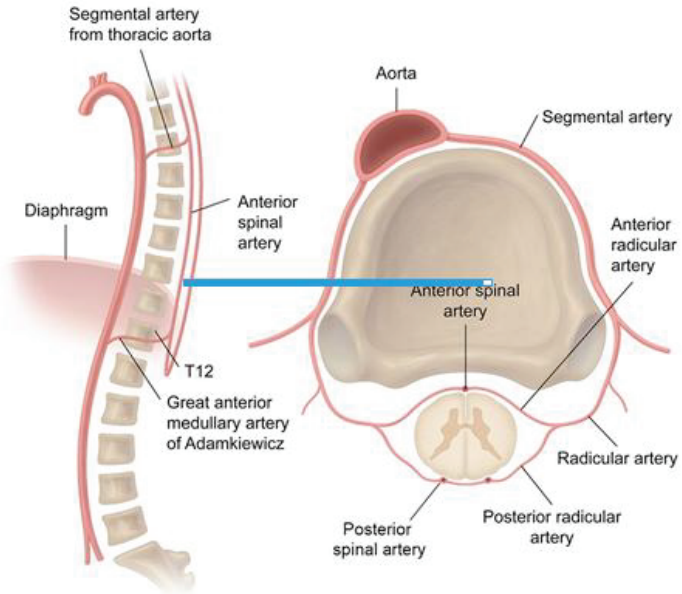
pain, temperature &

Exhibit Display

Blood supply of the spinal cord

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(Choice B) Complete loss of all lower extremity sensation (due to injury of the STTs and dorsal columns)



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**(Choice B)** Complete loss of all lower extremity sensation (due to injury of the STTs and dorsal columns) and motor function (due to injury of the CSTs) may be seen in complete SC injury, as can occur in SC transection.

**(Choices C and E)** An isolated defect of crude touch sensation or pain/temperature sensation could occur only with isolated injury to the anterior or lateral STT, respectively. Because the anterior spinal artery also supplies the tracts (eg, CSTs) surrounding the STTs, it is extremely uncommon to have bilateral injury to only the anterior or lateral STT.

**(Choice D)** Diminished proprioception and motor function can occur with simultaneous injury to the dorsal columns and CSTs. A classic cause is subacute combined degeneration of the dorsal and lateral SC white matter, which is seen in vitamin $B_{12}$ deficiency.

**(Choice F)** Selective loss of proprioceptive (along with vibratory and light touch) sensation occurs with isolated injury of the bilateral dorsal columns. A classic example is tabes dorsalis, a form of tertiary neurosyphilis that causes damage to the dorsal columns and dorsal nerve roots.

**Educational objective:**
Ischemia of the anterior two-thirds of the spinal cord can occur with disruption of the anterior spinal artery blood supply. The resulting anterior cord syndrome causes bilateral distal loss of pain, temperature, and


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(Choice B) Complete loss of all lower extremity sensation (due to injury of the STTs and dorsal columns)

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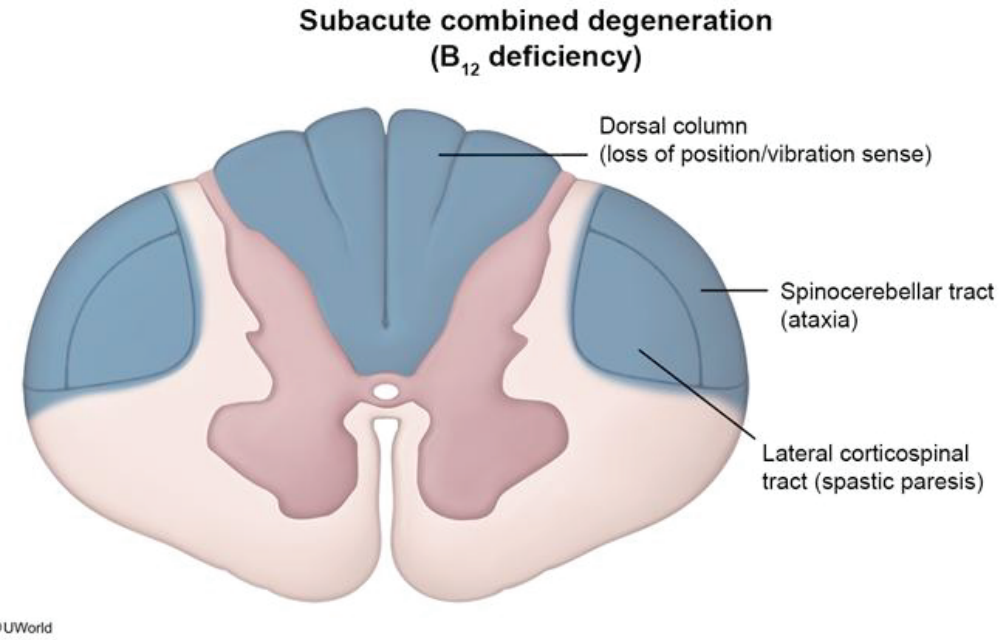


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(Choice B) Complete loss of all lower extremity sensation (due to injury of the STTs and dorsal columns)

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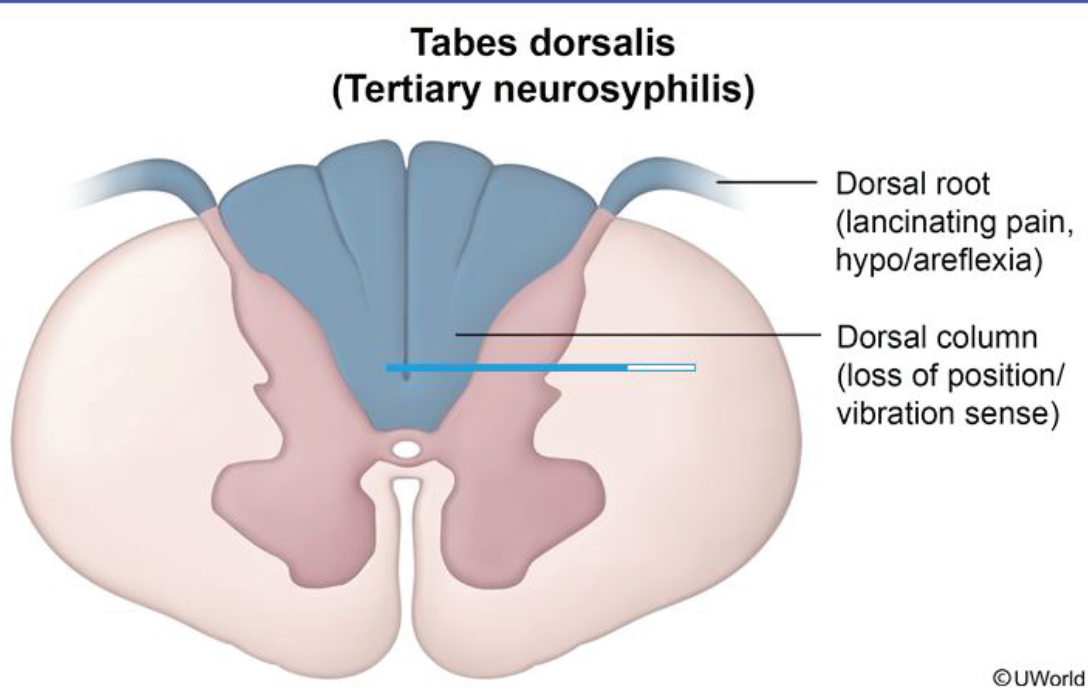


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only the anterior or lateral STT.

**(Choice D)** Diminished proprioception and motor function can occur with simultaneous injury to the dorsal columns and CSTs. A classic cause is subacute combined degeneration of the dorsal and lateral SC white matter, which is seen in vitamin $B_{12}$ deficiency.

**(Choice F)** Selective loss of proprioceptive (along with vibratory and light touch) sensation occurs with isolated injury of the bilateral dorsal columns. A classic example is tabes dorsalis, a form of tertiary neurosyphilis that causes damage to the dorsal columns and dorsal nerve roots.

**Educational objective:**

Ischemia of the anterior two-thirds of the spinal cord can occur with disruption of the anterior spinal artery blood supply. The resulting anterior cord syndrome causes bilateral distal loss of pain, temperature, and crude touch sensation (from injury to the spinothalamic tracts) and paralysis (from injury to the lateral corticospinal tracts).

**References**

- Incomplete cord syndromes: clinical and imaging review.
- Spinal cord injury following thoracic and thoracoabdominal repairs.



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A 45-year-old man comes to the clinic due to a 2-month history of progressive left arm clumsiness and weakness. The patient initially attributed his symptoms to a left rotator cuff injury he sustained several years ago; however, he has recently developed problems with his gait. The patient's symptoms have interfered with daily activities such as bathing and dressing. He has had no recent injury, headaches, or bowel/bladder symptoms. On physical examination, there is reduced muscle strength in the left upper extremity. Further evaluation with brain MRI reveals a lesion involving the corticospinal tract. Which of the following additional signs is most likely to been seen in this patient?

A. Hyperactive deep tendon reflexes
B. Muscle atrophy
C. Muscle fasciculation
D. Muscle hypotonia
E. Resting tremor
F. Sensory loss in the affected area


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weakness. The patient initially attributed his symptoms to a left rotator cuff injury he sustained several years ago; however, he has recently developed problems with his gait. The patient's symptoms have interfered with daily activities such as bathing and dressing. He has had no recent injury, headaches, or bowel/bladder symptoms. On physical examination, there is reduced muscle strength in the left upper extremity. Further evaluation with brain MRI reveals a lesion involving the corticospinal tract. Which of the following additional signs is most likely to been seen in this patient?

- ✓ A. Hyperactive deep tendon reflexes (74%)
- B. Muscle atrophy (7%)
- C. Muscle fasciculation (7%)
- D. Muscle hypotonia (6%)
- E. ~~Resting tremor~~ (1%)
- F. ~~Sensory loss in the affected area~~ (3%)

Correct

74%
Answered correctly

02 mins, 22 secs
Time Spent

11/21/2020
Last Updated



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| | |
|---|---|
| **Upper motor neuron signs** | • Spastic paralysis<br>• Clasp-knife rigidity<br>• Hyperreflexia<br>• Babinski sign |
| **Lower motor neuron signs** | • Flaccid paralysis<br>• Hypotonia<br>• Hyporeflexia<br>• Muscle atrophy & fasciculations |

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Voluntary muscle activity is mediated by the **corticospinal (pyramidal) tracts**. First-order neurons of these tracts are located in the premotor and motor cortex of the frontal lobe (Brodmann areas 6 and 4, respectively). Their efferent fibers descend through the internal capsule, midbrain, and pons, and continue to form the pyramids on the anterior aspect of the medulla. In the medulla, 90% of the fibers decussate (cross) to form the lateral corticospinal tract. Fibers that do not decussate descend as the anterior corticospinal tract. The axons of both tracts synapse on the motor neurons of the anterior horn (second-order neurons). Damage to the corticospinal tract is divided into upper and lower motor neuron lesions:

1. **Upper motor neuron** (UMN) refers to anything above the anterior horn. Lesions to UMNs (eg, due to


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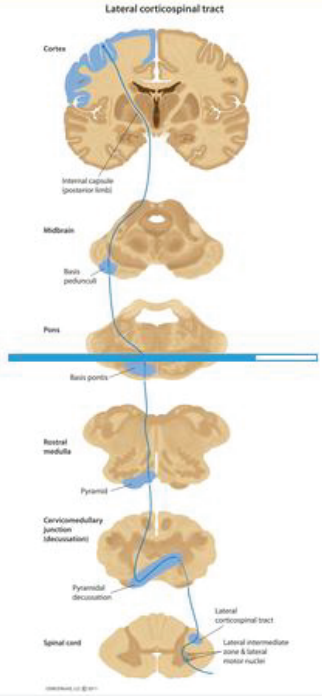


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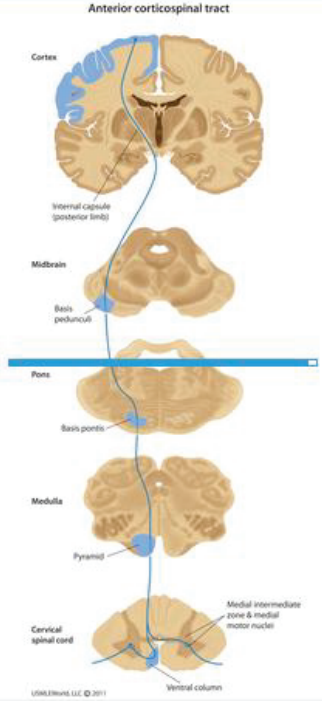


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order neurons). Damage to the corticospinal tract is divided into upper and lower motor neuron lesions:

1. **Upper motor neuron** (UMN) refers to anything above the anterior horn. Lesions to UMNs (eg, due to stroke, brain tumor) cause a combination of **spastic paralysis**, clasp-knife **rigidity, hyperreflexia** (including clonus), and upgoing plantar reflexes (**Babinski sign**). This likely occurs due to loss of descending inhibition over second-order neurons in the anterior horn.
2. Damage to the motor neurons of the anterior horn is considered a lower motor neuron (LMN) lesion. This type of injury leads to flaccid paralysis, hypotonia, hyporeflexia, muscle atrophy, and fasciculations. Poliomyelitis and infantile spinal muscular atrophy are examples of LMN lesions **(Choices B, C, and D)**.

Combined UMN and LMN lesions are characteristic of amyotrophic lateral sclerosis (Lou Gehrig disease).

**(Choice E)** Resting tremor is characteristic of Parkinson disease, which occurs due to loss of dopaminergic neurons in the substantia nigra.

**(Choice F)** Sensory information is transmitted by the spinothalamic tract (pain and temperature) and dorsal column pathway (vibration and proprioception). Lesions to the corticospinal tract do not cause sensory deficits.

**Educational objective:**


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**(Choices B, C, and D)**.

Combined UMN and LMN lesions are characteristic of amyotrophic lateral sclerosis (Lou Gehrig disease).

**(Choice E)** Resting tremor is characteristic of Parkinson disease, which occurs due to loss of dopaminergic neurons in the substantia nigra.

**(Choice F)** Sensory information is transmitted by the spinothalamic tract (pain and temperature) and dorsal column pathway (vibration and proprioception). Lesions to the corticospinal tract do not cause sensory deficits.

**Educational objective:**

Upper motor neuron damage leads to spastic paralysis, hyperreflexia, and an upgoing plantar reflex (Babinski sign) due to loss of descending inhibition over lower motor neurons in the anterior horn. Conversely, lower motor neuron lesions cause flaccid paralysis, hypotonia, hyporeflexia, muscle atrophy, and fasciculations.

**References**


- Spastic hypertonia and movement disorders: pathophysiology, clinical presentation, and quantification.
- The pathophysiology of spasticity.




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A 42-year-old homeless man comes to the emergency department due to painful muscle spasms. The patient has had frequent involuntary contractions of the jaw, neck, and trunk muscles, which are triggered by sensory stimuli. He has a history of injection drug use and has had several injection site infections. Physical examination shows neck stiffness and decreased opening of the jaw. Which of the following is the most likely path taken by the agent responsible for this patient's condition?

A. Bite wound → peripheral nerves → CNS neurons

B. Contaminated food → systemic circulation → presynaptic nerve terminals

C. Infected wound → systemic circulation → brain parenchyma

D. Nasopharyngeal exudate → systemic circulation → neurons

E. Oral mucosa → trigeminal nerve → temporal lobe

F. Puncture wound → motor neurons → spinal cord interneurons

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A 42-year-old homeless man comes to the emergency department due to painful muscle spasms. The patient has had frequent involuntary contractions of the jaw, neck, and trunk muscles, which are triggered by sensory stimuli. He has a history of injection drug use and has had several injection site infections. Physical examination shows neck stiffness and decreased opening of the jaw. Which of the following is the most likely path taken by the agent responsible for this patient's condition?

A. Bite wound → peripheral nerves → CNS neurons (8%)

B. ~~Contaminated food → systemic circulation → presynaptic nerve terminals~~ (4%)

C. Infected wound → systemic circulation → brain parenchyma (8%)

D. ~~Nasopharyngeal exudate → systemic circulation → neurons~~ (1%)

E. ~~Oral mucosa → trigeminal nerve → temporal lobe~~ (1%)

F. Puncture wound → motor neurons → spinal cord interneurons (75%)

Incorrect
Correct answer

75%
Answered correctly

02 mins
Time Spent

02/03/2021
Last Updated



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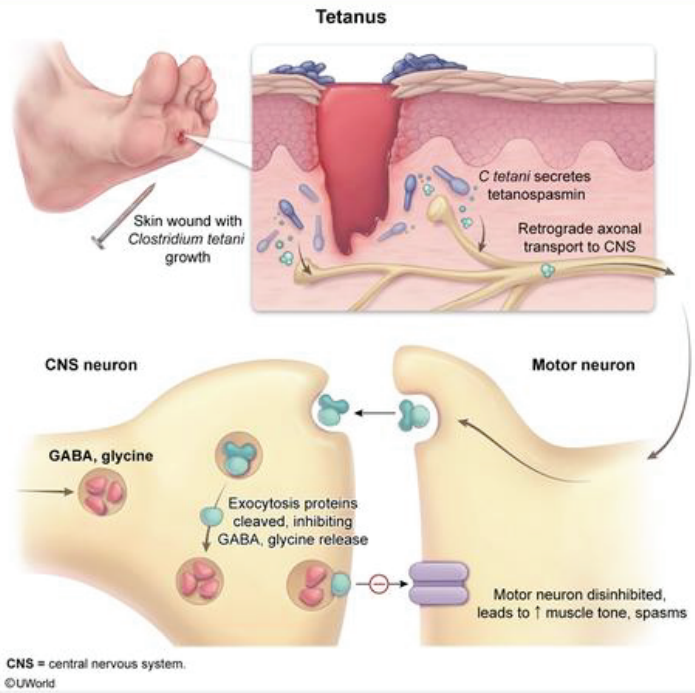


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This patient with painful muscle spasms and neck/jaw contraction likely has **tetanus**, which is caused by the spore-forming anaerobic bacterium *Clostridium tetani*. *C tetani* spores are found in soil worldwide and are typically transmitted to humans during a **puncture injury** (eg, dirty needle use, splinter). The low oxygen tension of a puncture wound allows spores to germinate into vegetative rod-shaped bacteria that proliferate locally and produce tetanospasmin (**tetanus toxin**).

Although the pathogen is noninvasive (it stays localized to the wound site), the toxin enters the presynaptic terminals of the lower **motor neurons** and travels by retrograde axonal transport to the CNS. In the spinal cord, at the level of the anterior horn cells, the toxin **blocks inhibitory interneurons**, leading to spasmodic muscle contraction. Classic findings include jaw stiffness due to masseter muscle spasm (trismus/lockjaw) and sustained contraction of the facial muscles, producing a bizarre "smiling" appearance (risus sardonicus). Spasmodic contraction of the back and neck can cause opisthotonos, and respiratory muscle involvement that can lead to respiratory failure.

**(Choice A)** Rabies virus is transmitted via the saliva of an infected animal during a bite wound. The virus spreads by retrograde axonal transport through peripheral nerves and enters the spinal cord/CNS. Patients with rabies usually develop painful pharyngeal spasms, hydrophobia, fever, and hyperactivity. However, this patient has no history of an animal bite; he likely developed tetanus due to a puncture wound with a contaminated needle.


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with a contaminated needle.

**(Choice B)** Food-borne botulism is marked by the ingestion of preformed botulism toxin with subsequent spread through the systemic circulation. The toxin blocks cholinergic presynaptic nerve terminals, which results in symmetric, descending weakness.

**(Choice C)** Bacteria (eg, *Staphylococcus aureus*) from a wound can spread through the bloodstream to the brain leading to brain abscess. Symptoms vary but the most common manifestation is unilateral headache.

**(Choice D)** Diphtheria is associated with the formation of a pseudomembranous pharyngeal exudate and the elaboration of diphtheria toxin into the systemic circulation. The toxin causes cardiac (myocarditis) and neurologic toxicity.

**(Choice E)** Herpes simplex virus type 1 causes orolabial lesions and is the most frequent cause of sporadic encephalitis, which occurs when the virus spreads via the olfactory tract to the temporal lobe (olfactory cortex). Patients usually present with confusion, fever, focal neurologic deficits, and seizures.

**Educational objective:**

Tetanus is caused by infection with toxigenic strains of the anaerobic bacterium *Clostridium tetani*. Transmission typically occurs when spores are inoculated into the skin via a puncture wound. The bacteria


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the brain leading to brain abscess. Symptoms vary but the most common manifestation is unilateral headache.

**(Choice D)** Diphtheria is associated with the formation of a pseudomembranous pharyngeal exudate and the elaboration of diphtheria toxin into the systemic circulation. The toxin causes cardiac (myocarditis) and neurologic toxicity.

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**Educational objective:**
Tetanus is caused by infection with toxigenic strains of the anaerobic bacterium *Clostridium tetani*. Transmission typically occurs when spores are inoculated into the skin via a puncture wound. The bacteria germinate, replicate locally, and elaborate tetanospasmin (tetanus toxoid). The toxin spreads in a retrograde fashion through the lower motor neurons to the spinal cord, where it blocks inhibitory interneurons and causes spasmodic muscle contraction (eg, trismus, risus sardonicus).

| Microbiology | Nervous System | Tetanus |
|---|---|---|
| Subject | System | Topic |


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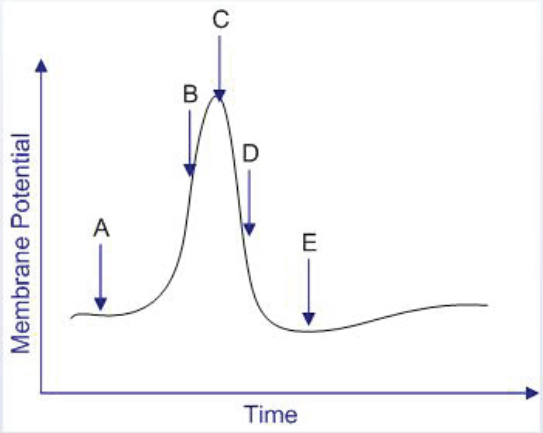
A 34-year-old man comes to the emergency department complaining of weakness, dizziness, and paresthesias involving his face and extremities. He has never had symptoms like this before. Two hours earlier, he ate fish at a new Japanese restaurant. Neurological examination shows reduced muscle strength and decreased deep-tendon reflexes. Which of the following parts of the action potential curve is most likely impaired in this patient?

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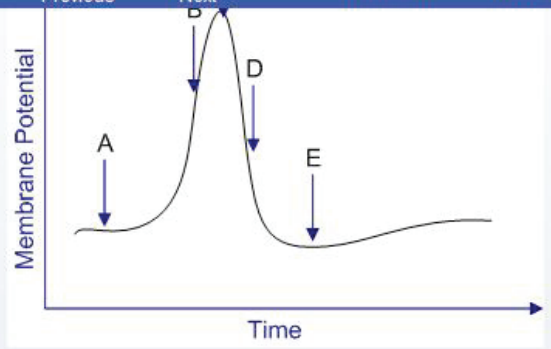


- A.A
- B.B
- C.C
- D.D
- E.E

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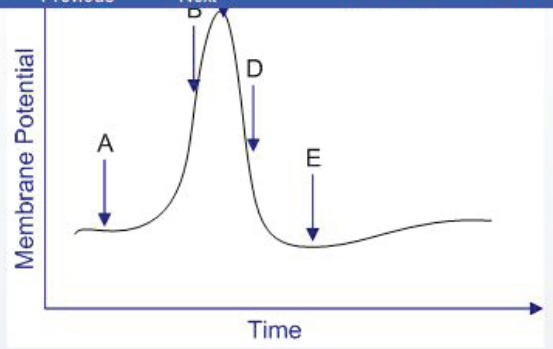


- A.A (7%)
- ✓ B.B (74%)
- C.C (5%)
- D.D (8%)
- E.E (4%)

Correct

74%

01 min

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| Voltage-gated sodium channel toxins | |
|---|---|
| Tetrodotoxin (puffer fish) | Binds to $Na^+$ channels, inhibiting $Na^+$ influx and preventing action potential conduction |
| Saxitoxin (dinoflagellates in "red tide") | |
| Ciguatoxin (exotic fish, Moray eel) | Binds to the $Na^+$ channel, keeping it open and causing persistent depolarization |
| Batrachotoxin (South American frogs) | |

This patient's constellation of symptoms (ie, paresthesias, weakness, dizziness, nausea) and history of fish consumption are strongly suggestive of food poisoning by pufferfish, a Japanese delicacy. Pufferfish can be lethal if not properly prepared. It is necessary to remove the organs containing high quantities of tetrodotoxin, a toxin produced by microorganisms associated with the fish.

Tetrodotoxin binds to voltage-gated sodium channels in nerve and cardiac tissue, preventing sodium influx


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Tetrodotoxin binds to voltage-gated sodium channels in nerve and cardiac tissue, preventing sodium influx and depolarization. Symptoms of tetrodotoxin poisoning occur quickly after ingestion and include dizziness, weakness, loss of reflexes, paresthesias of the face and extremities, nausea, vomiting, and diarrhea. Higher exposures can cause severe hypotension and general paralysis; death can occur from respiratory failure and hypotension. Treatment includes supportive care and intestinal decontamination with gut lavage and charcoal.

**(Choice A)** The resting potential is equal to approximately -70 mV. It is maintained by high membrane $K^+$ permeability and low $Na^+$ permeability. $K^+$ efflux occurs via non-gated $K^+$ channels (leak channels).

**(Choice C)** Overshoot represents the maximal value of the action potential during which the membrane potential is positive. At this point, open sodium channels become inactivated and close, preventing further increase in the membrane potential.

**(Choice D)** Repolarization results from closure of $Na^+$ channels and simultaneous opening of $K^+$ channels. This results in a sharp decrease in $Na^+$ conductance and a significant increase in $K^+$ conductance. Potassium efflux is responsible for returning the membrane potential to the resting potential.

**(Choice E)** Hyperpolarization occurs for a short moment following repolarization due to the slow closure of voltage-gated potassium channels. The membrane potential becomes more negative than the normal


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increase in the membrane potential.

**(Choice D)** Repolarization results from closure of $Na^+$ channels and simultaneous opening of $K^+$ channels. This results in a sharp decrease in $Na^+$ conductance and a significant increase in $K^+$ conductance. Potassium efflux is responsible for returning the membrane potential to the resting potential.

**(Choice E)** Hyperpolarization occurs for a short moment following repolarization due to the slow closure of voltage-gated potassium channels. The membrane potential becomes more negative than the normal resting potential and approaches the $K^+$ equilibrium potential of -85 mV. When the voltage-gated $K^+$ channels close, the membrane potential returns to the resting value.

**Educational objective:**

Pufferfish poisoning is caused by tetrodotoxin, a neurotoxin produced by microorganisms associated with the fish. Tetrodotoxin binds to voltage-gated sodium channels in nerve and cardiac tissue, preventing sodium influx and depolarization.

**References**

- Tetrodotoxin: a brief history



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A 26-year-old previously healthy man is brought to the emergency department following a motorbike accident. He is found to have a maxillofacial injury. His condition is stabilized, and surgical repair is performed. While recovering, the patient develops difficulty chewing food. On examination, the jaw deviates to the right side when the patient is instructed to open his mouth. The nerve that has been injured in this patient exits the skull through which of the following foramina?

A. Foramen lacerum
B. Foramen ovale
C. Foramen rotundum
D. Foramen spinosum
E. Jugular foramen

Submit



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A 26-year-old previously healthy man is brought to the emergency department following a motorbike accident. He is found to have a maxillofacial injury. His condition is stabilized, and surgical repair is performed. While recovering, the patient develops difficulty chewing food. On examination, the jaw deviates to the right side when the patient is instructed to open his mouth. The nerve that has been injured in this patient exits the skull through which of the following foramina?

- A. Foramen lacerum (2%)
- ✓ B. Foramen ovale (62%)
- C. Foramen rotundum (21%)
- D. Foramen spinosum (8%)
- E. Jugular foramen (5%)

Correct

62% Answered correctly

01 min, 03 secs Time Spent

10/02/2020 Last Updated



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| | Skull foramen | Traversing structures |
|---|---|---|
| **Anterior cranial fossa** | Cribriform plate | CN I olfactory bundles |
| **Middle cranial fossa** | Optic canal | CN II, ophthalmic artery, central retinal vein |
| | Superior orbital fissure | CN III, IV, $V_1$, VI, ophthalmic vein, sympathetic fibers |
| | Foramen rotundum | CN $V_2$ (maxillary) |
| | Foramen ovale | CN $V_3$ (mandibular) |
| | Foramen spinosum | Middle meningeal artery & vein |
| **Posterior** | Internal acoustic meatus | CN VII, VIII |
| | Jugular foramen | CN IX, X, XI, jugular vein |


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| | | |
|---|---|---|
| | Foramen spinosum | Middle meningeal artery & vein |
| **Posterior cranial fossa** | Internal acoustic meatus | CN VII, VIII |
| | Jugular foramen | CN IX, X, XI, jugular vein |
| | Hypoglossal canal | CN XII |
| | Foramen magnum | Spinal roots of CN XI, brain stem, vertebral arteries |

**CN** = cranial nerve.

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This patient has symptoms consistent with injury of the **third division of the trigeminal nerve** (cranial nerve [CN] V3, mandibular nerve), which provides sensory innervation to the face and motor innervation to the muscles of mastication. These include the 3 muscles that close the jaw (masseter, medial pterygoid, temporalis) and the single muscle that opens the jaw (lateral pterygoid).

Unilateral injury to CN V3 will result in unopposed action of the **contralateral** pterygoid muscles; because of the plane of action of these muscles, this leads to deviation of the mandible **toward** the paralyzed side on opening the mouth. Bilateral paralysis would cause mandibular drop and lack of jaw movement. CN V3


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on opening the mouth. Bilateral paralysis would cause mandibular drop and lack of jaw movement. CN V3 exits the skull through the foramen ovale, which also contains the lesser petrosal nerve, the accessory meningeal artery, and the emissary veins.

The **second division** of the trigeminal nerve (CN V2, maxillary nerve) exits the skull via the **foramen rotundum (Choice C)**. The foramen spinosum contains the middle meningeal artery, middle meningeal vein, and the meningeal (recurrent) branch of CN V3, which supplies the dura and contains sympathetic fibers **(Choice D)**. The **first branch** of the trigeminal nerve (CN V1, ophthalmic nerve) passes through the **superior orbital fissure**.

**(Choice A)** The foramen lacerum contains only a few small vessels (meningeal branch of ascending pharyngeal artery, emissary veins) and is otherwise occluded by fibrous tissue and cartilage. The internal carotid artery passes along its superior surface but does not traverse it.

**(Choice E)** The jugular foramen contains CNs IX, X, and XI; the inferior petrosal and sigmoid sinuses; and the posterior meningeal artery.

**Educational objective:**
The third (mandibular) branch of the trigeminal nerve exits the skull through the foramen ovale and innervates the muscles of mastication, including the masseter, the medial and lateral pterygoids, and the temporalis muscles.


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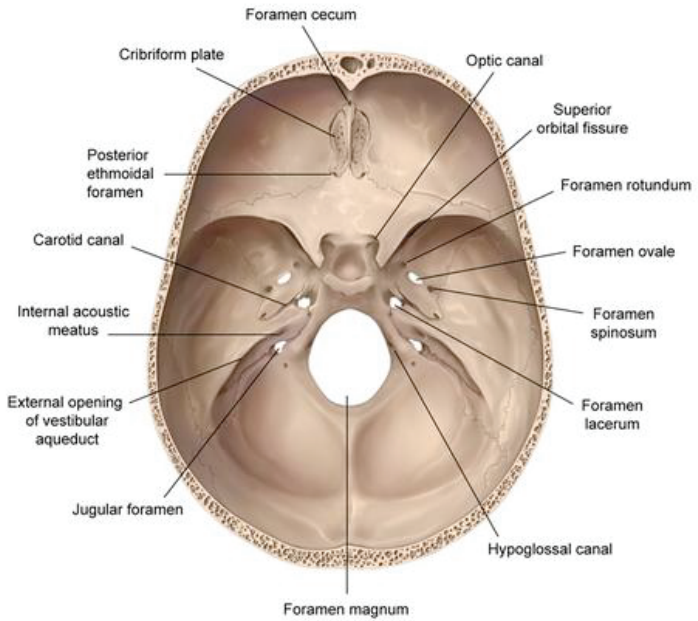
on opening the mouth. Bilateral paralysis would cause mandibular drop and lack of jaw movement. CN V3

Exhibit Display

Foramina of the cranial base

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vein, and the meningeal (recurrent) branch of CN V3, which supplies the dura and contains sympathetic fibers **(Choice D)**. The **first branch** of the trigeminal nerve (CN V1, ophthalmic nerve) passes through the **superior orbital fissure**.

**(Choice A)** The foramen lacerum contains only a few small vessels (meningeal branch of ascending pharyngeal artery, emissary veins) and is otherwise occluded by fibrous tissue and cartilage. The internal carotid artery passes along its superior surface but does not traverse it.

**(Choice E)** The jugular foramen contains CNs IX, X, and XI; the inferior petrosal and sigmoid sinuses; and the posterior meningeal artery.

**Educational objective:**
The third (mandibular) branch of the trigeminal nerve exits the skull through the foramen ovale and innervates the muscles of mastication, including the masseter, the medial and lateral pterygoids, and the temporalis muscles.

| Anatomy | Nervous System | Trigeminal nerve |
|---|---|---|
| Subject | System | Topic |

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A 59-year-old man comes to the office for evaluation of a facial skin lesion. The lesion is a mole-like spot that has been on the patient's face for the past several months and has slowly enlarged. He reports no pain or bleeding from the lesion. Family medical history is positive for skin cancer. Physical examination findings are shown in the exhibit. Biopsy of the lesion with a local nerve block for anesthesia is planned. Which of the following injection sites is most likely to provide adequate anesthesia for the procedure?

A. Infraorbital foramen
B. Mandibular foramen
C. Mental foramen
D. Stylomastoid foramen
E. Superior orbital fissure

Submit



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Exhibit Display

**Basal cell carcinoma**

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A 59-year-old man comes to the office for evaluation of a facial skin lesion. The lesion is a mole-like spot that has been on the patient's face for the past several months and has slowly enlarged. He reports no pain or bleeding from the lesion. Family medical history is positive for skin cancer. Physical examination findings are shown in the exhibit. Biopsy of the lesion with a local nerve block for anesthesia is planned. Which of the following injection sites is most likely to provide adequate anesthesia for the procedure?

- A. Infraorbital foramen (57%)
- B. ~~Mandibular foramen~~ (15%)
- C. ~~Mental foramen~~ (7%)
- D. Stylomastoid foramen (11%)
- E. ~~Superior orbital fissure~~ (7%)

Correct

57%
Answered correctly

55 secs
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01/21/2021
Last Updated



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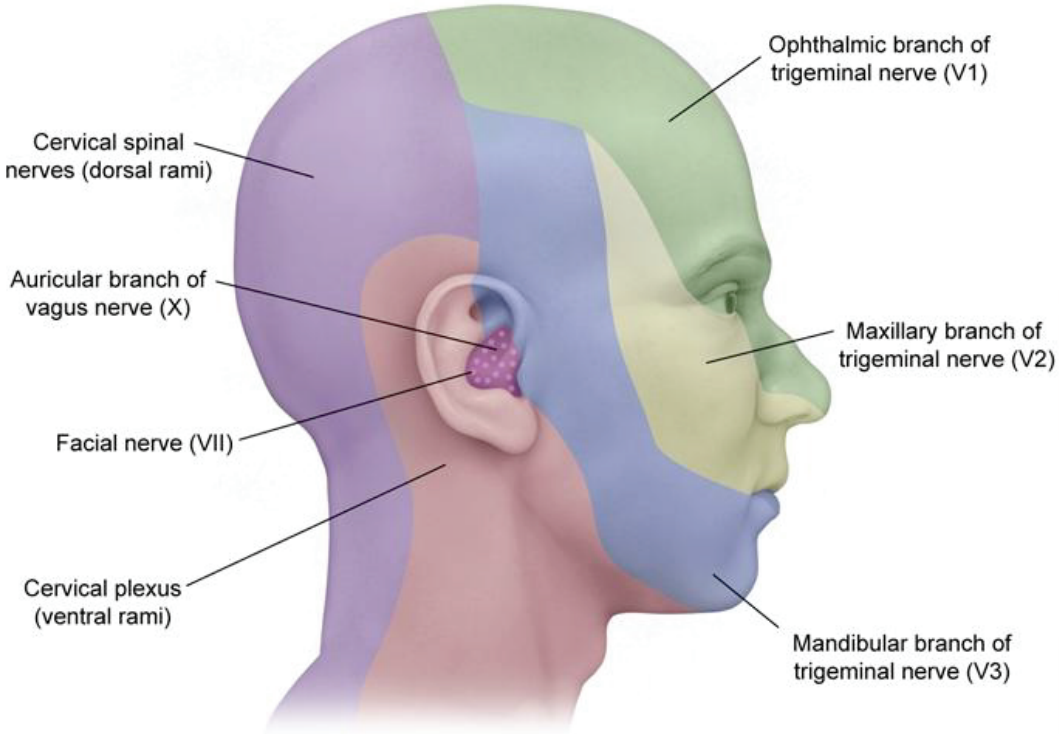
## Dermatomes of head & neck



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This patient is undergoing excision of a skin lesion located on his cheek, just lateral to his nose, in an area supplied by the **maxillary branch of the trigeminal nerve** (CN V2). Nerve blocks are often performed using bony landmarks (eg, foramina) as an anatomic guide. The trigeminal nerve divides into 3 branches that then travel as follows:

- Ophthalmic nerve (CN V1): exits the cranium through the superior orbital fissure **(Choice E)**, passes superiorly along the orbit, and then exits the orbit through the frontal bone via the supraorbital foramen.
- **Maxillary nerve** (CN V2): leaves the skull through the foramen rotundum and then traverses the pterygopalatine fossa to enter the maxilla via the infraorbital canal. It then exits the facial bones through the **infraorbital foramen**. The infraorbital artery also runs along the infraorbital groove and canal and exits the infraorbital foramen together with the infraorbital nerve.
- Mandibular nerve (CN V3): exits the cranium through the foramen ovale. One branch (the inferior alveolar nerve) enters the mandibular foramen **(Choice B)** on the internal surface of the mandible and then exits at the mental foramen **(Choice C)** at the anterior mandible.

A more general maxillary nerve (CN V2) block can be performed at the pterygopalatine fossa near where the nerve exits the skull at the foramen rotundum, but it is technically more difficult and will also block other



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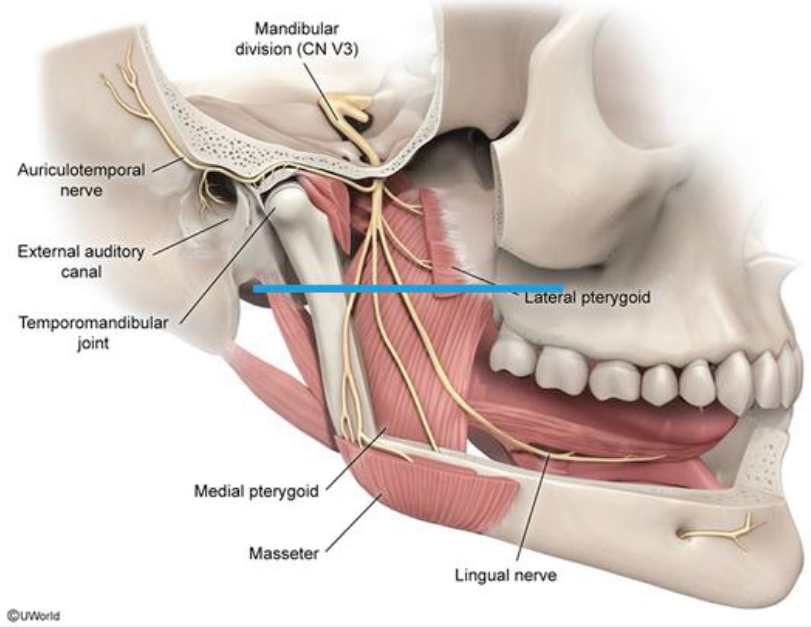
Exhibit Display

Mandibular division of trigeminal nerve

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the nerve exits the skull at the foramen rotundum, but it is technically more difficult and will also block other



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alveolar nerve) enters the mandibular foramen **(Choice B)** on the internal surface of the mandible and then exits at the mental foramen **(Choice C)** at the anterior mandible.

A more general maxillary nerve (CN V2) block can be performed at the pterygopalatine fossa near where the nerve exits the skull at the foramen rotundum, but it is technically more difficult and will also block other maxillary branches (eg, zygomatic, palatine) in addition to the infraorbital nerve.

**(Choice D)** The facial nerve (CN VII) exits the skull at the stylomastoid foramen and provides motor innervation to the muscles of facial expression. It does not contribute to sensory innervation of the face.

**Educational objective:**

The maxillary division of the trigeminal nerve (CN V2) provides sensory innervation to the cheek. It passes through the foramen rotundum, then the pterygopalatine fossa, and then exits the maxilla through the infraorbital foramen. Nerve blocks to provide anesthesia to the cheek are frequently performed at the infraorbital foramen.

| Anatomy | Nervous System | Trigeminal nerve |
|---|---|---|
| Subject | System | Topic |

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A newborn is taken to the neonatal intensive care unit after delivery due to respiratory distress. The neonate was born full-term, and there were no significant complications during pregnancy or delivery. Once the patient is stabilized, a detailed physical examination is performed. The neonate has an underdeveloped mandible and hypoplastic zygomatic bones. Genetic testing confirms a gene mutation that results in abnormal development of the first and second pharyngeal arches. Which of the following structures is also likely abnormal in this patient?

A. Cricoid cartilage
B. Glossopharyngeal nerve
C. Greater horn of hyoid
D. Stapes
E. Thyroid cartilage
F. Vagus nerve

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A newborn is taken to the neonatal intensive care unit after delivery due to respiratory distress. The neonate was born full-term, and there were no significant complications during pregnancy or delivery. Once the patient is stabilized, a detailed physical examination is performed. The neonate has an underdeveloped mandible and hypoplastic zygomatic bones. Genetic testing confirms a gene mutation that results in abnormal development of the first and second pharyngeal arches. Which of the following structures is also likely abnormal in this patient?

A. Cricoid cartilage (5%)
B. ~~Glossopharyngeal nerve~~ (4%)
C. Greater horn of hyoid (11%)
D. Stapes (72%)
E. Thyroid cartilage (5%)
F. ~~Vagus nerve~~ (0%)


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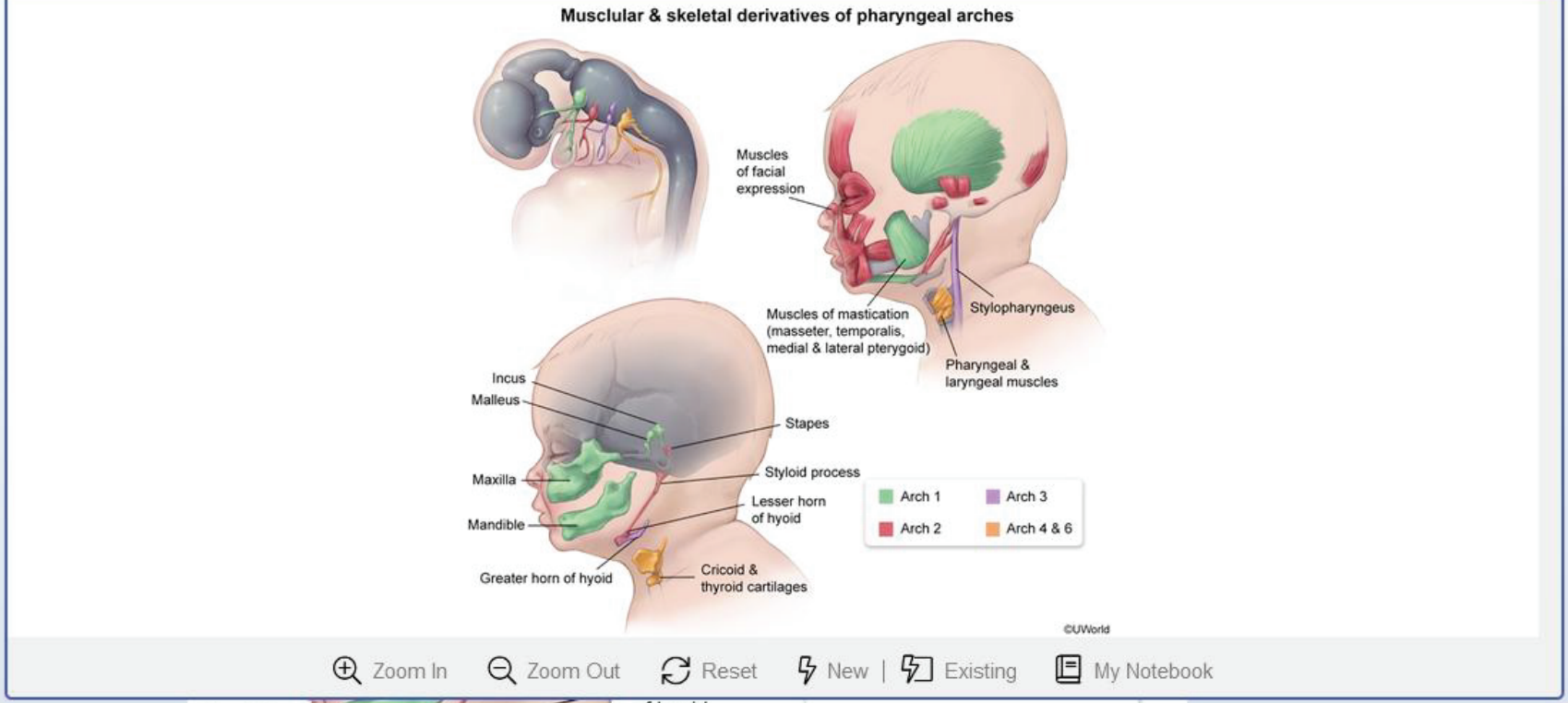
Musclular & skeletal derivatives of pharyngeal arches

Exhibit Display



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The developing embryo has 6 pharyngeal or branchial arches, all but the fifth arch contribute to adult structures. The mesoderm forms muscular and vascular elements, and neural crest cells form the bony and cartilaginous structures. Each arch is also innervated by a specific cranial nerve (CN).

The **first pharyngeal arch** is associated with the trigeminal nerve (CN V). Its bony derivatives include the **maxilla, zygoma, mandible, incus,** and **malleus**; its muscular derivatives include the muscles of mastication (eg, masseter, temporalis). The **second pharyngeal arch** is associated with the facial nerve (CN VII) and gives rise to the **styloid process of the temporal bone, lesser horn of the hyoid,** and **stapes**. Muscular derivatives of the second arch include the muscles of facial expression.

This neonate's presentation is consistent with **Treacher-Collins syndrome** (TCS), a genetic disorder resulting in the abnormal development of the first and second pharyngeal arches. The craniofacial abnormalities (eg, mandibular, maxillary, and zygomatic bone hypoplasia) often result in airway compromise and feeding difficulties. In addition, absent or abnormal ossicles (eg, incus, malleus, stapes) lead to profound conductive hearing loss.

**(Choices A and E)** The fourth and sixth arches make up the cartilaginous structures of the larynx, including the cricoid and thyroid cartilages.


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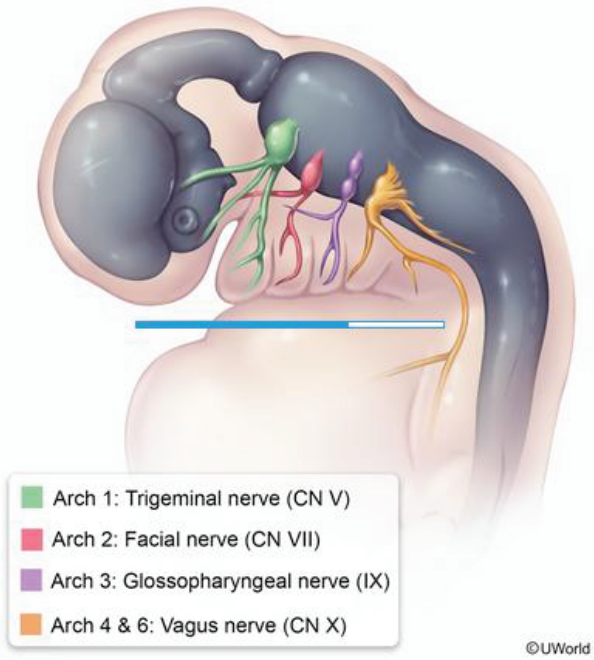
Exhibit Display

## Pharyngeal arches in the embryo

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**(Choice B)** The glossopharyngeal nerve (CN IX) is derived from the third pharyngeal arch. Dysfunction may lead to impaired taste perception and an absent gag reflex.

**(Choice C)** The hyoid bone at the base of the mandible is derived from 2 pharyngeal arches. The lesser horn of the hyoid is derived from the second arch, and the greater horn of the hyoid is derived from the third arch.

**(Choice F)** The vagus nerve (CN X) is derived from the fourth and sixth arches. Dysfunction results in laryngeal and pharyngeal paralysis and autonomic dysfunction (eg, esophageal motility, gastric acid secretion, heart rate variability).

**Educational objective:**

The development of derivatives of the first (eg, trigeminal nerve, mandible, maxilla, zygoma, incus, malleus) and second (eg, facial nerve, stapes, styloid process, lesser horn of hyoid) pharyngeal arches can be disrupted in genetic disorders (eg, Treacher-Collins syndrome), resulting in hypoplasia of the mandibular and zygomatic bones.

**References**

- First and second brachial arch syndromes: multimodality approach



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A researcher is studying autopsy findings in patients diagnosed with neurodegenerative disorders. In some of the brain specimens, a neuronal protein that primarily exists in an alpha-helical secondary structure is found to be in a beta-sheet conformation. The altered protein is resistant to protease and has accumulated in large quantities within the cells. Further investigation shows that the abnormal isoform can perpetually induce the same conformational change within normally folded proteins. Which of the following histopathological changes are most likely present in the brains of these patients?

A. Discrete, demyelinated plaques and gliosis
B. Intranuclear inclusions in oligodendrocytes
C. Microglial nodules and multinucleated giant cells
D. Neurofibrillary tangles and neuritic plaques
E. Sponge-like vacuolated neurons in gray matter

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A researcher is studying autopsy findings in patients diagnosed with neurodegenerative disorders. In some of the brain specimens, a neuronal protein that primarily exists in an alpha-helical secondary structure is found to be in a beta-sheet conformation. The altered protein is resistant to protease and has accumulated in large quantities within the cells. Further investigation shows that the abnormal isoform can perpetually induce the same conformational change within normally folded proteins. Which of the following histopathological changes are most likely present in the brains of these patients?

A. ~~Discrete, demyelinated plaques and gliosis~~ (0%)

B. ~~Intranuclear inclusions in oligodendrocytes~~ (0%)

C. ~~Microglial nodules and multinucleated giant cells~~ (0%)

D. Neurofibrillary tangles and neuritic plaques (29%)

✓ E. Sponge-like vacuolated neurons in gray matter (68%)

Correct

68%
Answered correctly

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Time Spent

03/19/2021
Last Updated



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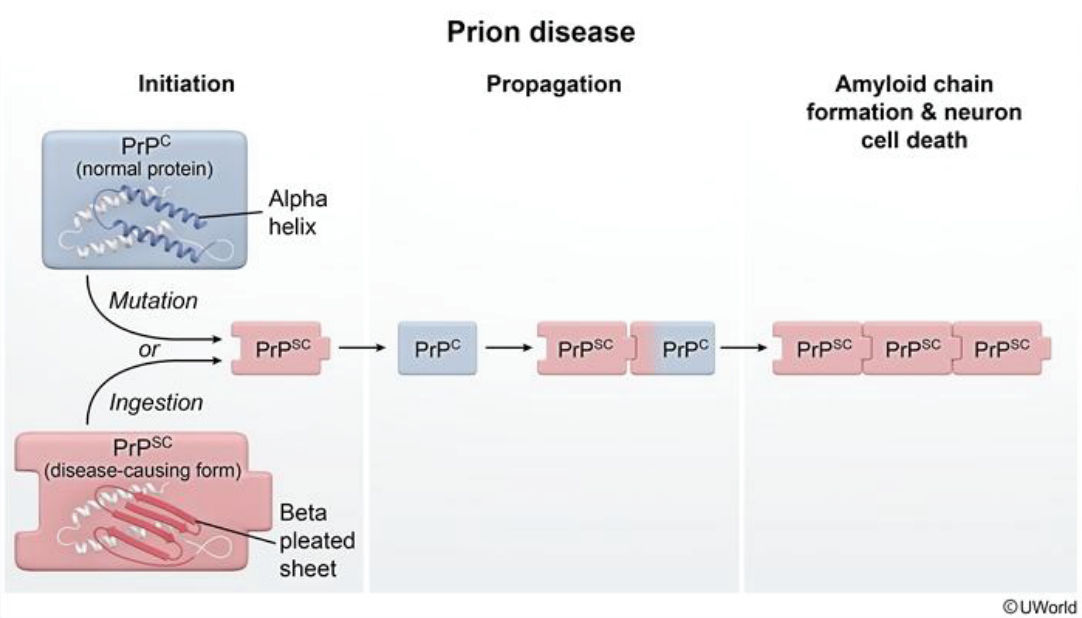


**Prion diseases** are progressive **neurodegenerative** disorders caused by accumulation of an abnormally folded protein within the brain. Prion diseases are seen in both humans (eg, Creutzfeldt-Jacob, fatal familial insomnia, Kuru) and animals (eg, scrapie, bovine spongiform encephalopathy) and may be transmitted between species with ingestion of tainted meat (eg, variant Creutzfeldt-Jacob).


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transmitted between species with ingestion of tainted meat (eg, variant Creutzfeldt-Jakob).

Prion proteins are found in both neuronal and non-neuronal brain cells and normally exist in an **alpha-helical structure** ($PrP^{c}$). Prion disease occurs after a domain in this protein undergoes a **conformation change** from an alpha helix into **beta-pleated sheet** isoform ($PrP^{Sc}$ [scrapie]), which confers the ability to induce similar conformational changes in other proteins. This beta sheet conformation is **resistant to proteases** and forms long, highly **neurotoxic** fibrils, which accumulate intracellularly in neurons and form extracellular deposits.

On microscopy, there is **spongiform degeneration** of the gray matter, which is characterized by formation of **microscopic vacuoles** within the neuronal processes. Neuronal loss, reactive gliosis, and cystic expansion of vacuoles occur as the disease progresses. Extracellular prion accumulations (Kuru plaques) are also frequently present and stain positive with Congo-red and periodic acid–Schiff stains.

**(Choice A)** Discrete, demyelinated plaques and gliosis are seen in multiple sclerosis, in which autoreactive T lymphocytes, microglia, and plasma cells react to antigens in myelin.

**(Choice B)** Progressive multifocal leukoencephalopathy is a demyelinating disease caused by reactivation of the JC virus; intranuclear inclusions within oligodendrocytes and large, bizarre astrocytes are typical findings.



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**(Choice C)** Microglial nodules form when cells of microglia surround a neuron and phagocytize it. These structures, along with multinucleated giant cells, are characteristic of viral infections of the CNS. They are found in HIV-associated encephalopathy.

**(Choice D)** Neurofibrillary tangles and neuritic plaques are seen in Alzheimer disease. Hyperphosphorylation of tau protein results in neurofibrillary tangles, and decreased clearance of amyloid-beta results in senile plaques. However, these proteins cannot induce similar conformational changes in normal proteins.

**Educational objective:**
Prion diseases are rapidly progressive neurodegenerative disorders caused by the accumulation of an abnormally folded protein within the brain. Prion proteins are normally found in an alpha helix form; a conformation change into a beta-sheet form confers resistance to proteases and can trigger similar conformational changes in other normally folded proteins. Characteristic microscopic findings include spongiform degeneration of the gray matter with vacuolization of neurons, gliosis, and cyst formation.

| Pathology | Nervous System | Prion disease |
|---|---|---|
| Subject | System | Topic |


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A 23-year-old female is brought to the ER after having a tonic-clonic seizure. She has a history of seizures and takes phenytoin. She does not use tobacco, alcohol or illicit drugs. On physical examination, no focal abnormalities are noted. Blood tests reveal her plasma phenytoin level to be low. She states that she has been compliant with her medication. Which of the following drugs may be responsible for this patient's condition if co-administered with phenytoin?

A. Amoxicillin
B. Rifampin
C. Metronidazole
D. Fluconazole
E. Cimetidine
F. Omeprazole
G. Oral contraceptives



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A 25-year-old female is brought to the ER after having a tonic-clonic seizure. She has a history of seizures and takes phenytoin. She does not use tobacco, alcohol or illicit drugs. On physical examination, no focal abnormalities are noted. Blood tests reveal her plasma phenytoin level to be low. She states that she has been compliant with her medication. Which of the following drugs may be responsible for this patient's condition if co-administered with phenytoin?

A. ~~Amoxicillin~~ (0%)
B. Rifampin (65%)
C. ~~Metronidazole~~ (1%)
D. ~~Fluconazole~~ (3%)
E. ~~Cimetidine~~ (13%)
F. ~~Omeprazole~~ (2%)
G. ~~Oral contraceptives~~ (12%)

Correct

65%
Answered correctly

57 secs
Time Spent

01/10/2021
Last Updated



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As with many other medications, phenytoin is metabolized by hepatic P450 oxidase. Plasma drug level, efficacy, and the severity of side effects are directly influenced by the rate of metabolism of phenytoin. The following features of phenytoin metabolism are important:

1. Hepatic hydroxylation of phenytoin is **dose-dependent.** When low doses of phenytoin are administered, a sufficient number of enzyme molecules are available, and the drug is eliminated rapidly. Higher doses of phenytoin may fully saturate the enzyme; hence, increasing the dose above the saturation limit causes an inability to metabolize the drug and a rapid rise in plasma levels. Even a small increase in phenytoin intake above the prescribed dose may lead to severe toxicity.
2. Phenytoin is **an inducer of P450 oxidase**. Induction of this enzyme increases the consumption of many medications that are metabolized by the liver, such as oral contraceptives. When the P450 oxidase system is induced, the serum concentration of such medications will decrease, thereby reducing efficacy.
3. Because phenytoin is metabolized by P450 enzymes, its level is affected when it is co-administered with other medications that induce or inhibit the P450 system. The co-administration of phenytoin with P450 inducers decreases concentration of phenytoin in plasma and diminishes its effectiveness. Some **P450 inducers** are barbiturates, rifampin, carbamazepine, griseofulvin, and chronic alcohol


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with other medications that induce or inhibit the P450 system. The co-administration of phenytoin with P450 inducers decreases concentration of phenytoin in plasma and diminishes its effectiveness.

Some **P450 inducers** are barbiturates, rifampin, carbamazepine, griseofulvin, and chronic alcohol consumption. P450 inhibitors slow hepatic metabolism, which increases the toxicity of phenytoin.

Some of **P450 inhibitors** are isoniazid, cimetidine, macrolides, azole antifungals, and grapefruit juice.

**(Choices A)** Amoxicillin do not affect the hepatic metabolism of phenytoin.

**(Choices C and G)** Both metronidazole and oral contraceptives are metabolized by hepatic P450 oxidase, but these two drugs neither induce nor inhibit the activity of P450 oxidase.

**(Choices D, E and F)** Fluconazole, cimetidine, and omeprazole inhibit P450 enzymes and increase the concentration of phenytoin in the serum.

**Educational objective:**

Phenytoin metabolism depends on the function of hepatic P450 oxidases and is dose-dependent. Drugs that induce hepatic microsomal enzymes (phenobarbital, carbamazepine, and rifampin) enhance phenytoin metabolism and decrease its serum concentration. You should know all of the commonly-prescribed medications that are metabolized by the P450 system, and you should know which drugs induce or inhibit the function of these enzymes.



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A 68-year-old man is brought to the emergency department by his daughter due to change in mental status. Over the past 2 days, the patient has started seeing strangers sneaking around the house despite only he and his daughter being at home. He has also been intermittently confused, difficult to rouse, and distractible. The patient has had no headaches or focal weakness. He has no history of psychiatric illness but has been taking a sleep aid due to insomnia for the past week. Temperature is 36.7 C (98 F), blood pressure is 140/85 mm Hg, pulse is 88/min, and respirations are 12/min. On physical examination, the patient is somnolent but rousable to voice. He is not oriented to place or time. Pupils are bilaterally equal and reactive to light. Bilateral upper and lower extremity muscle strength, deep tendon reflexes, and pain sensation are normal. Blood cell counts and serum chemistry studies are within normal limits. Which of the following is the most likely diagnosis?

A. Acute ischemic stroke
B. Brief psychotic disorder
C. Dementia with Lewy bodies
D. Frontotemporal dementia
E. Medication-induced delirium



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distractible. The patient has had no headaches or focal weakness. He has no history of psychiatric illness but has been taking a sleep aid due to insomnia for the past week. Temperature is 36.7 C (98 F), blood pressure is 140/85 mm Hg, pulse is 88/min, and respirations are 12/min. On physical examination, the patient is somnolent but rousable to voice. He is not oriented to place or time. Pupils are bilaterally equal and reactive to light. Bilateral upper and lower extremity muscle strength, deep tendon reflexes, and pain sensation are normal. Blood cell counts and serum chemistry studies are within normal limits. Which of the following is the most likely diagnosis?

A. Acute ischemic stroke
B. Brief psychotic disorder
C. Dementia with Lewy bodies
D. Frontotemporal dementia
E. Medication-induced delirium
F. Occult bacterial infection

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distractible. The patient has had no headaches or focal weakness. He has no history of psychiatric illness but has been taking a sleep aid due to insomnia for the past week. Temperature is 36.7 C (98 F), blood pressure is 140/85 mm Hg, pulse is 88/min, and respirations are 12/min. On physical examination, the patient is somnolent but rousable to voice. He is not oriented to place or time. Pupils are bilaterally equal and reactive to light. Bilateral upper and lower extremity muscle strength, deep tendon reflexes, and pain sensation are normal. Blood cell counts and serum chemistry studies are within normal limits. Which of the following is the most likely diagnosis?

A. ~~Acute ischemic stroke~~ (0%)
B. Brief psychotic disorder (3%)
C. Dementia with Lewy bodies (10%)
D. Frontotemporal dementia (2%)
E. Medication-induced delirium (81%)
F. ~~Occult bacterial infection~~ (1%)


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This patient's acute onset of fluctuating altered mental status (eg, impaired attention, change in level of consciousness, hallucinations, disorientation) in the context of recent initiation of a sleep aid is consistent with **medication-induced delirium**. Delirium is a disorder of attention and general cognition that has an **acute onset** and follows a **fluctuating course**. Delirium is frequently multifactorial and is most commonly caused by an acute medical illness, adverse effect of a medication, or drug intoxication/withdrawal.

**Elderly** patients are at **increased risk** for delirium, and medications with a high risk of precipitating delirium (eg, sedative-hypnotics [eg, zolpidem], benzodiazepines, opioids, anticholinergic agents) must be used with extreme caution in this patient population. Elderly patients with baseline dementia are even more vulnerable to delirium. The definitive treatment for delirium involves addressing the underlying cause (eg, treating the medical illness, removing the offending medication).

**(Choice A)** Acute ischemic stroke rarely causes acute delirium, especially without the presence of focal neurological deficits.

**(Choice B)** Brief psychotic disorder may be diagnosed in patients with ≥1 day but <1 month of psychotic symptoms (which are not better explained by the effects of a medication or medical illness). Patients with brief psychotic disorder are typically fully oriented.



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brief psychotic disorder are typically fully oriented.

**(Choice C)** Dementia with Lewy bodies is a neurodegenerative disorder characterized by progressive dementia, fluctuating cognition, parkinsonian symptoms, REM sleep behavior disorder, and visual hallucinations.

**(Choice D)** Frontotemporal dementia is a progressive neurodegenerative disease that classically presents with early and prominent behavioral disturbances (eg, impulsivity, disinhibition, apathy) with subsequent progressive decline in executive function, memory, and language function.

**(Choice F)** Although an occult bacterial infection may precipitate delirium, this patient's normal laboratory results, vital signs, and physical examination; absence of systemic symptoms; and recent initiation of a drug known to cause delirium make medication-induced delirium a better explanation for his symptoms.

**Educational objective:**
Delirium is characterized by the acute onset of fluctuating disturbance in attention and general cognition (eg, altered level of consciousness, disorientation, hallucinations). Common medications that may precipitate delirium in high-risk populations (eg, elderly patients) include sedative-hypnotics, benzodiazepines, opioids, and anticholinergic medications.

**References**



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A 43-year-old male with multiple medical problems including seizure disorder and mental illness comes to your office for the first time in order to establish a primary care physician. On routine physical examination, you notice the findings shown in the photo below.

Which of the following is most likely responsible for the condition of this patient's teeth and gums?

A. Phenytoin



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Which of the following is most likely responsible for the condition of this patient's teeth and gums?

A. Phenytoin
B. Lithium
C. Prednisone
D. Cocaine
E. Methimazole
F. Clozapine

Submit



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Which of the following is most likely responsible for the condition of this patient's teeth and gums?

- A. Phenytoin (82%) ✓
- B. Lithium (5%)
- C. Prednisone (1%)
- D. Cocaine (4%)
- E. Methimazole (2%)
- F. Clozapine (3%)

Correct

82%

15 secs

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Gingival hyperplasia, like that shown in the photo above, is a common side effect of phenytoin. It occurs in 50% of patients who have had 3-4 months of phenytoin therapy. The mechanism of this side effect is associated with increased expression of platelet-derived growth factor (PDGF). When gingival macrophages are exposed to increased amounts of PDGF, they stimulate proliferation of gingival cells and alveolar bone. Gingival hyperplasia may regress after discontinuation of phenytoin.

Phenytoin is an anticonvulsant effective in the treatment of grand mal (tonic-clonic) seizures, partial seizures, and status epilepticus. Phenytoin inhibits abnormal electrical activity of the brain by blocking voltage-gated sodium channels in neurons. Phenytoin has a narrow therapeutic index with a number of potential adverse effects:

1. Phenytoin toxicity is mainly characterized by CNS manifestations. Its effect on the cerebellum and vestibular system can cause ataxia and nystagmus.
2. Long-term therapy with phenytoin may cause gingival hyperplasia, coarsening of the facial features, and hirsutism.
3. Phenytoin interferes with the metabolism of folic acid and may cause megaloblastic anemia.
4. Phenytoin induces the P450 cytochrome oxidase system. It increases the metabolism—and therefore decreases the blood level—of many medications.



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3. Phenytoin interferes with the metabolism of folic acid and may cause megaloblastic anemia.
4. Phenytoin induces the P450 cytochrome oxidase system. It increases the metabolism—and therefore decreases the blood level—of many medications.
5. If taken during pregnancy, phenytoin may cause fetal hydantoin syndrome.

**(Choice B)** Lithium also has a narrow therapeutic index. Lithium toxicity is associated with neuromuscular excitability (irregular coarse tremors, fascicular twitching, rigid motor agitation, and ataxia). It may also cause nephrogenic diabetes insipidus, hypothyroidism, and cardiac conduction defects, but not gingival hyperplasia.

**(Choice C)** The adverse effects of prednisone include hyperglycemia, weight gain, depression, fluid retention with edema, and osteoporosis.

**(Choice D)** Cocaine blocks the re-uptake of norepinephrine, serotonin, and dopamine in the CNS. It can cause cardiac ischemia, hypertension, and seizures. Cocaine withdrawal is associated with severe depression.

**(Choice E)** Methimazole inhibits thyroid hormone synthesis by suppressing the iodination and coupling of tyrosine. Side effects include edema, rash, and agranulocytosis.

**(Choice F)** Clozapine is an atypical antipsychotic that is most helpful in treating the negative symptoms of


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**(Choice D)** Cocaine blocks the re-uptake of norepinephrine, serotonin, and dopamine in the CNS. It can cause cardiac ischemia, hypertension, and seizures. Cocaine withdrawal is associated with severe depression.

**(Choice E)** Methimazole inhibits thyroid hormone synthesis by suppressing the iodination and coupling of tyrosine. Side effects include edema, rash, and agranulocytosis.

**(Choice F)** Clozapine is an atypical antipsychotic that is most helpful in treating the negative symptoms of schizophrenia. The most serious side effects of clozapine include agranulocytosis and seizures.

**Educational Objective:**
Gingival hyperplasia is a common side effect of phenytoin and is sometimes reversible when phenytoin is withdrawn. Phenytoin causes increased expression of platelet-derived growth factor (PDGF). When gingival macrophages are exposed to increased amounts of PDGF, they stimulate proliferation of gingival cells and alveolar bone. Phenytoin toxicity mainly affects the cerebellum and vestibular system, causing ataxia and nystagmus.

| Pharmacology | Nervous System | Antiepileptics |
|---|---|---|
| Subject | System | Topic |



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A 34-year-old man comes to the emergency department due to severe headache. The patient describes unbearable, throbbing pain around his right eye that awakened him. Over the past week, he has had several similar episodes, which spontaneously resolved after 20-30 minutes. He has no other medical conditions and takes no medications. The patient smokes a pack of cigarettes daily and drinks alcohol on social occasions. On physical examination, he appears restless and paces in the room. There is mild conjunctival injection and miosis of the right eye. Neurologic examination shows no abnormalities. Which of the following is the most likely cause of this patient's current symptoms?

A. Cavernous sinus thrombosis
B. Cluster headache
C. Migraine without aura
D. Opiate withdrawal
E. Trigeminal neuralgia
F. Vertebrobasilar ischemia



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unbearable, throbbing pain around his right eye that awakened him. Over the past week, he has had several similar episodes, which spontaneously resolved after 20-30 minutes. He has no other medical conditions and takes no medications. The patient smokes a pack of cigarettes daily and drinks alcohol on social occasions. On physical examination, he appears restless and paces in the room. There is mild conjunctival injection and miosis of the right eye. Neurologic examination shows no abnormalities. Which of the following is the most likely cause of this patient's current symptoms?

A. Cavernous sinus thrombosis (7%)
B. Cluster headache (81%)
C. Migraine without aura (3%)
D. Opiate withdrawal (2%)
E. Trigeminal neuralgia (4%)
F. Vertebrobasilar ischemia (0%)

Correct

81%
Answered correctly

48 secs
Time Spent

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| | Types of headache | | |
|---|---|---|---|
| | **Migraine** | **Cluster** | **Tension** |
| **Sex predilection** | Female > male | Male > female | Female > male |
| **Family history** | Often present | ± | None |
| **Onset** | Variable | During sleep or similar timing daily | Under stress |
| **Location** | Often unilateral | Behind one eye | Band-like pattern around the head (bilateral) |
| **Character** | Pulsatile & throbbing | Excruciating, sharp & steady (ie, "ice-pick") | Dull, tight & persistent |
| **Duration** | 4-72 hours | 15-180 minutes | 30 minutes to months/years |



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|---|---|---|---|
| | | | months/years |
| **Associated symptoms** | Photophobia, phonophobia & nausea, ± aura | Ipsilateral sweating, facial flushing, nasal congestion, pupillary changes & lacrimation | Muscle tenderness in the head, neck, or shoulders |

This young man with throbbing, unilateral periorbital headache associated with conjunctival injection and miosis has **cluster headaches**. The pathogenesis of cluster headaches is poorly understood but likely includes genetic predisposition, vascular dilation, and activation of the trigeminal-autonomic reflex. Males are affected more commonly than females.

Cluster headaches present with rapid-onset, severe, **unilateral periorbital** and temporal pain; patients are often restless or agitated during episodes. **Ipsilateral autonomic symptoms** due to parasympathetic hyperactivity are common and include nasal congestion, lacrimation, ptosis, miosis, and conjuntival injection. The headaches typically last 15-180 minutes and tend to occur in clusters (often at the same time each day, even if asleep) over a period of several weeks.

**(Choice A)** Cavernous sinus thrombosis typically occurs in patients with thrombophilia (eg, malignancy, antithrombin deficiency) or as a septic thrombosis related to a sinus infection or facial cellulitis. Orbital pain is common; however, it is typically worsened with eye movement. Periorbital swelling, fever, and proptosis


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**(Choice A)** Cavernous sinus thrombosis typically occurs in patients with thrombophilia (eg, malignancy, antithrombin deficiency) or as a septic thrombosis related to a sinus infection or facial cellulitis. Orbital pain is common; however, it is typically worsened with eye movement. Periorbital swelling, fever, and proptosis are other frequent findings.

**(Choice C)** Migraine without aura typically causes severe, pulsatile, unilateral headache often associated with photophobia, phonophobia, nausea, and vomiting. Miosis and lacrimation are unexpected.

**(Choice D)** Opiate withdrawal can cause lacrimation, rhinorrhea, and diaphoresis, but would usually cause bilateral symptoms. It typically also causes gastrointestinal symptoms (eg, diarrhea, nausea), piloerection, and mydriasis; orbital pain is unexpected.

**(Choice E)** Trigeminal neuralgia (tic douloureux) causes sudden, "electric" pain in the distribution of the maxillary and/or mandibular divisions of the trigeminal nerve, often preceded by light touch. Episodes last for seconds and do not typically occur during sleep.

**(Choice F)** Vertebrobasilar ischemia can cause headaches but also typically causes dizziness, double vision or vision loss, and ataxia.

**Educational objective:**

Cluster headaches cause severe, episodic, unilateral periorbital and temporal pain associated with



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**(Choice D)** Opiate withdrawal can cause lacrimation, rhinorrhea, and diaphoresis, but would usually cause bilateral symptoms. It typically also causes gastrointestinal symptoms (eg, diarrhea, nausea), piloerection, and mydriasis; orbital pain is unexpected.

**(Choice E)** Trigeminal neuralgia (tic douloureux) causes sudden, "electric" pain in the distribution of the maxillary and/or mandibular divisions of the trigeminal nerve, often preceded by light touch. Episodes last for seconds and do not typically occur during sleep.

**(Choice F)** Vertebrobasilar ischemia can cause headaches but also typically causes dizziness, double vision or vision loss, and ataxia.

**Educational objective:**
Cluster headaches cause severe, episodic, unilateral periorbital and temporal pain associated with ipsilateral autonomic symptoms (eg, lacrimation, nasal congestion, miosis, conjunctival injection). The headaches typically last 15-180 minutes and tend to occur in clusters (often at the same time each day). Males are affected more commonly than females.

| Pathology | Nervous System | Cluster headache |
|---|---|---|
| Subject | System | Topic |


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A 55-year-old man is being evaluated for a 4-week history of right shoulder pain. The pain worsens when actively abducting the shoulder or when lying on the shoulder at night. The patient also has weakness with abduction and external rotation of the right shoulder. He has attempted treatment with over-the-counter analgesics with limited relief. MRI of the shoulder shows a partial rotator cuff tear, and the patient is scheduled for surgical repair. Immediately before the surgery, he receives anesthesia with an injection between the right anterior and middle scalene muscles in order to block the C3 through C7 nerve roots of the cervical and brachial plexuses. Which of the following muscles is most likely to be paralyzed due to the anesthesia?

A. Cricothyroid
B. Diaphragm
C. Intercostal
D. Platysma
E. Sternocleidomastoid



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actively abducting the shoulder or when lying on the shoulder at night. The patient also has weakness with abduction and external rotation of the right shoulder. He has attempted treatment with over-the-counter analgesics with limited relief. MRI of the shoulder shows a partial rotator cuff tear, and the patient is scheduled for surgical repair. Immediately before the surgery, he receives anesthesia with an injection between the right anterior and middle scalene muscles in order to block the C3 through C7 nerve roots of the cervical and brachial plexuses. Which of the following muscles is most likely to be paralyzed due to the anesthesia?

A. Cricothyroid (2%)
B. Diaphragm (69%)
C. Intercostal (4%)
D. Platysma (6%)
E. Sternocleidomastoid (17%)

Correct

69%
Answered correctly

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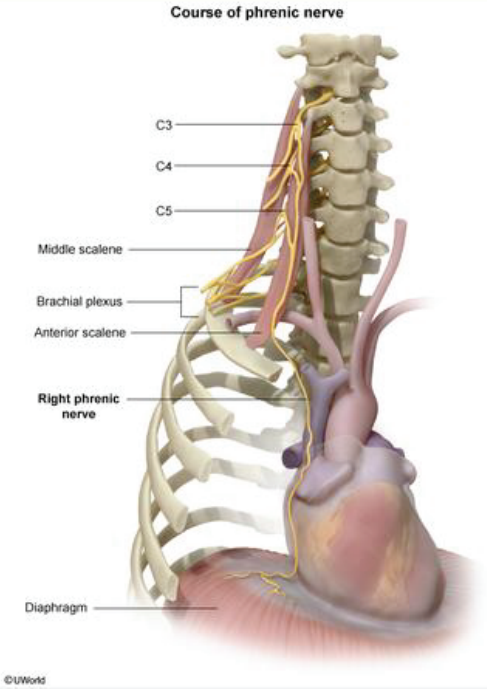


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The brachial plexus originates from the C5-T1 spinal nerve roots, which combine into 3 trunks and pass between the **anterior and middle scalene muscles** (scalene triangle) in the posterior neck. The trunks then differentiate into divisions, cords, and terminal nerve branches. The brachial plexus supplies all sensory and motor innervation to the upper extremity, except for an area of skin near the axilla which is innervated by the intercostobrachial nerve and the trapezius muscle which is innervated by the accessory nerve (CN XI).

An **interscalene nerve block** is a regional anesthesia technique used for procedures involving the **shoulder and upper arm**. In this technique, anesthetic is administered to the brachial plexus roots and trunks between the anterior and middle scalene muscles. Anesthetic also traverses along the interscalene sheath and affects the roots of the **phrenic nerve (C3-C5)**, which causes transient **ipsilateral diaphragmatic paralysis**. Therefore, an interscalene nerve block should be avoided in patients with conditions that could be worsened by unilateral diaphragmatic paralysis (eg, chronic lung disease, contralateral phrenic nerve dysfunction).

**(Choice A)** The cricothyroid muscle is innervated by the external branch of the superior laryngeal nerve (vagus nerve [CN X]) and helps tense the vocal cords, allowing higher-pitched speech.



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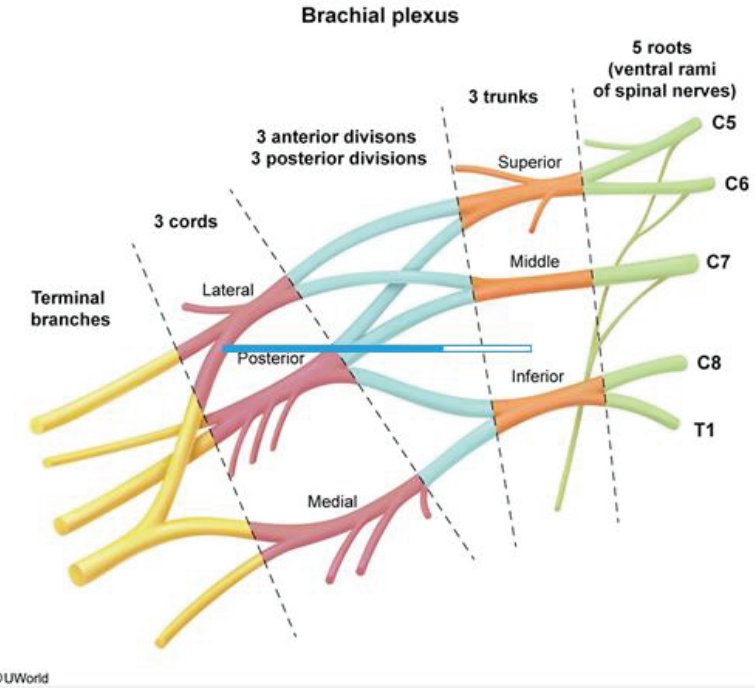


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(vagus nerve [CN X]) and helps tense the vocal cords, allowing higher-pitched speech.



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contralateral phrenic nerve dysfunction).

**(Choice A)** The cricothyroid muscle is innervated by the external branch of the superior laryngeal nerve (vagus nerve [CN X]) and helps tense the vocal cords, allowing higher-pitched speech.

**(Choice C)** The intercostal muscles aid in expansion and contraction of the chest cavity during breathing. They are innervated by the intercostal nerves (ventral rami of thoracic spinal nerves).

**(Choice D)** The platysma is a superficial neck muscle that covers the anterior neck from the clavicle to the mandible and tenses the skin of the neck and lower face. It is innervated by the cervical branch of the facial nerve (CN VII).

**(Choice E)** The sternocleidomastoid, a superficial neck muscle controlling neck flexion and head rotation, is innervated by the accessory nerve (CN XI).

**Educational objective:**
An interscalene nerve block is used to provide anesthesia for the shoulder and upper arm by anesthetizing the upper brachial plexus (C5-C7) as it passes between the anterior and middle scalene muscles. Anesthetic also transverses along the interscalene sheath, frequently resulting in transient ipsilateral diaphragmatic paralysis due to involvement of the phrenic nerve roots (C3-C5).

**References**



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A 65-year-old woman is brought to the clinic by her husband due to worsening memory problems. She has a medical history significant for long-standing hypertension, type 2 diabetes mellitus, and depression. Physical examination shows cognitive impairment but no focal neurologic deficits. Two years later, the patient dies suddenly from a massive myocardial infarction. Congo red staining of brain samples obtained from the hippocampus and cerebral arterioles reveals patchy red deposits that turn yellow-green under polarized light. This patient most likely suffered from which of the following conditions?

A. Alzheimer disease
B. Huntington disease
C. Parkinson disease
D. Pick disease
E. Pseudodementia
F. Vascular dementia
G. Vitamin $B_{12}$ deficiency



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a medical history significant for long-standing hypertension, type 2 diabetes mellitus, and depression. Physical examination shows cognitive impairment but no focal neurologic deficits. Two years later, the patient dies suddenly from a massive myocardial infarction. Congo red staining of brain samples obtained from the hippocampus and cerebral arterioles reveals patchy red deposits that turn yellow-green under polarized light. This patient most likely suffered from which of the following conditions?

- A. Alzheimer disease (71%)
- B. ~~Huntington disease~~ (0%)
- C. ~~Parkinson disease~~ (0%)
- D. ~~Pick disease~~ (4%)
- E. Pseudodementia (2%)
- F. Vascular dementia (19%)
- G. ~~Vitamin $B_{12}$ deficiency~~ (0%)

Correct
71%
02 mins, 15 secs
01/13/2021


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**Amyloid** is an abnormally folded (insoluble) fibrillar protein that deposits in the extracellular space of tissues. When stained with Congo red and viewed under polarized light, these deposits have a characteristic apple-green birefringence due to their β-sheet structure. Amyloid deposition can affect multiple organ systems, as occurs with plasma cell tumors (eg, amyloid light chain protein [AL]) and chronic inflammatory diseases (eg, amyloid-associated protein [AA]).

However, in **Alzheimer disease**, amyloid deposits are seen exclusively in brain tissue. These deposits contain **beta-amyloid** (Aβ), which is formed by cleavage of amyloid precursor protein (a transmembrane glycoprotein). Early in the disease, neuritic (senile) plaques can be found in the medial temporal lobe (eg, hippocampus, amygdala, entorhinal cortex) and are composed of a central Aβ core surrounded by dystrophic neurites. Aβ deposition also occurs in the media/adventitia of cerebral vessels (amyloid angiopathy) and may cause vessel weakening with intracranial hemorrhage.

**(Choice B)** Huntington disease typically presents with dementia, choreiform movements, dystonia, and psychiatric symptoms. Patients characteristically have atrophy of the caudate and microscopy reveals intranuclear inclusions containing aggregates of huntingtin protein.

**(Choice C)** Parkinson disease usually presents with bradykinesia, rigidity, and tremor. Brain biopsy characteristically shows intracellular eosinophilic inclusions composed of α-synuclein (Lewy bodies).



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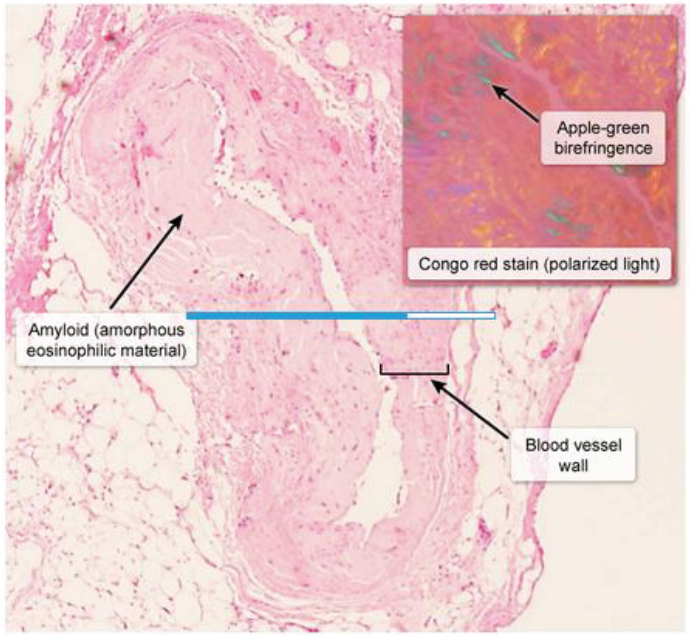
Exhibit Display

Amyloid

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characteristically shows intracellular eosinophilic inclusions composed of α-synuclein (Lewy bodies).



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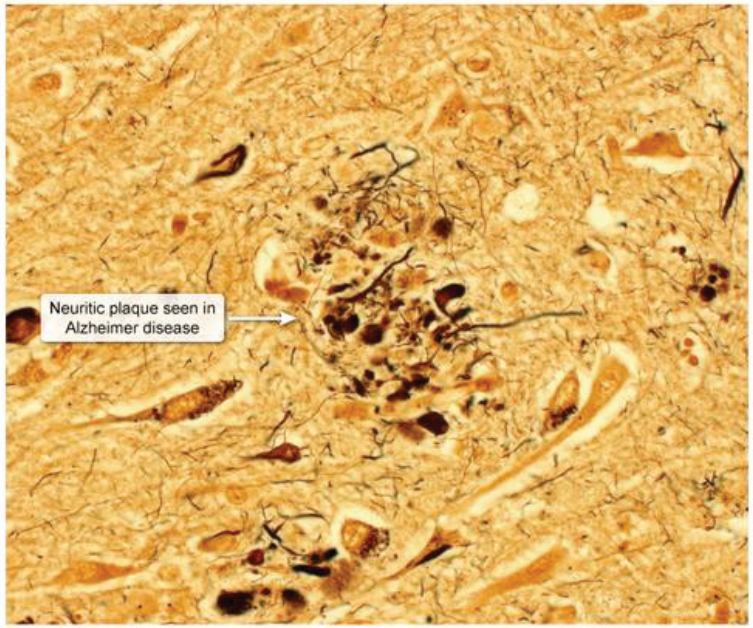
Alzheimer disease

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characteristically shows intracellular eosinophilic inclusions composed of α-synuclein (Lewy bodies).



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intranuclear inclusions containing aggregates of huntingtin protein.

**(Choice C)** Parkinson disease usually presents with bradykinesia, rigidity, and tremor. Brain biopsy characteristically shows intracellular eosinophilic inclusions composed of α-synuclein (Lewy bodies).

**(Choice D)** Pick disease (frontotemporal dementia) typically presents with changes in personality/behavior and abnormal speech (eg, aphasia). Individuals usually have pronounced frontotemporal brain atrophy, and silver staining shows round cytoplasmic inclusions containing aggregates of tau protein (Pick bodies).

**(Choice E)** Elderly individuals may develop cognitive impairment in association with depression ("pseudodementia"); however, neuritic plaques and amyloid angiopathy would not be seen.

**(Choice F)** Vascular dementia typically presents with sudden/stepwise cognitive decline in patients with cardiovascular risk factors and ischemic stroke. The absence of glial scar formation on autopsy makes vascular dementia less likely in this patient.

**(Choice G)** Vitamin $B_{12}$ deficiency is common in the elderly and may cause dementia, peripheral neuropathy, and/or subacute combined degeneration; however, neuritic plaques and amyloid angiopathy would not be seen.

**Educational objective:**

Amyloid is an abnormally folded (insoluble) extracellular protein that has apple-green birefringence when


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("pseudodementia"), however, neuritic plaques and amyloid angiopathy would not be seen.

**(Choice F)** Vascular dementia typically presents with sudden/stepwise cognitive decline in patients with cardiovascular risk factors and ischemic stroke. The absence of glial scar formation on autopsy makes vascular dementia less likely in this patient.

**(Choice G)** Vitamin $B_{12}$ deficiency is common in the elderly and may cause dementia, peripheral neuropathy, and/or subacute combined degeneration; however, neuritic plaques and amyloid angiopathy would not be seen.

**Educational objective:**
Amyloid is an abnormally folded (insoluble) extracellular protein that has apple-green birefringence when stained with Congo red and viewed under polarized light. Alzheimer disease is associated with beta-amyloid deposits in the brain parenchyma (neuritic plaques) and walls of cerebral vessels (amyloid angiopathy).

**References**

- Alzheimer's disease and the ß-amyloid peptide.

| Pathology | Nervous System | Alzheimer disease |
|---|---|---|
| Subject | System | Topic |



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A 9-year-old girl is brought to the emergency department following a 3-minute generalized seizure. She has had a fever with a worsening headache for 3 days. The girl has no medical problems and is not taking any medications. She lives with her parents and pet cat and has traveled to Canada and England. On physical examination, she is disoriented and has difficulty staying awake. Her speech is difficult to understand due to inappropriate word choice. She is admitted to the intensive care unit for further workup. The patient becomes unresponsive the following day and dies overnight. Autopsy reveals bilateral, hemorrhagic necrosis of the inferior and medial temporal lobes. This patient's condition was most likely caused by infection with which of the following?

A. Enterovirus
B. Herpes simplex virus
C. *Naegleria fowleri*
D. *Neisseria meningitidis*
E. *Streptococcus pneumoniae*
F. *Toxoplasma gondii*



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any medications. She lives with her parents and pet cat and has traveled to Canada and England. On physical examination, she is disoriented and has difficulty staying awake. Her speech is difficult to understand due to inappropriate word choice. She is admitted to the intensive care unit for further workup. The patient becomes unresponsive the following day and dies overnight. Autopsy reveals bilateral, hemorrhagic necrosis of the inferior and medial temporal lobes. This patient's condition was most likely caused by infection with which of the following?

A. Enterovirus (1%)
B. Herpes simplex virus (52%)
C. *Naegleria fowleri* (13%)
D. *Neisseria meningitidis* (4%)
E. *Streptococcus pneumoniae* (2%)
F. *Toxoplasma gondii* (24%)

Correct
52%
58 secs
01/05/2021



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| HSV encephalitis | |
|---|---|
| **Pathogenesis** | HSV-1 → olfactory tract → olfactory cortex (temporal lobe) |
| **Presentation** | Fever, headache, seizures, aphasia, mental status/behavior changes |
| **Diagnosis** | Temporal lobe hemorrhage/edema on brain imaging<br>Cerebrospinal fluid PCR for HSV |
| **Treatment** | Intravenous acyclovir |

**HSV-1** = herpes simplex virus type 1.

**Herpes simplex virus type 1 (HSV-1) encephalitis** is the most common cause of fatal sporadic encephalitis, or inflammation of the brain parenchyma. HSV-1 encephalitis results from **primary oropharyngeal infection** that travels via the olfactory tract or from the **reactivation of latent virus** in the trigeminal ganglion with subsequent spread into the cerebral vault. CT, MRI (red arrow), and post-mortem macroscopic brain examination reveal **edema and hemorrhagic necrosis of the temporal lobe**. Unilateral involvement is most common, but bilateral necrosis can also occur. Definitive diagnosis is made by polymerase chain reaction testing of cerebrospinal fluid.


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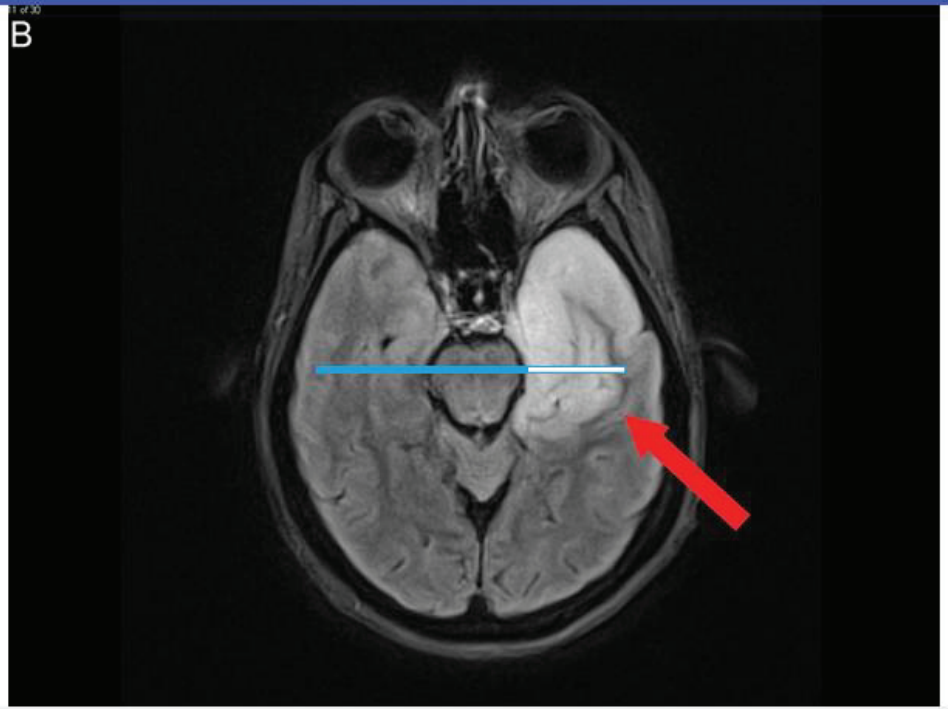


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by polymerase chain reaction testing of cerebrospinal fluid.

Symptoms of acute encephalitis include acute onset of **headache, fever, mental status changes** (eg, lethargy, disorientation), cranial nerve deficits (eg, Bell's palsy), and **seizures**. Temporal lobe damage can result in receptive **aphasia** and **personality changes** (eg, hypersexuality, aggression).

**(Choice A)** Enterovirus, particularly group B coxsackievirus, is the most common cause of viral meningitis in children. Less commonly, enterovirus causes encephalitis and acute flaccid paralysis, but temporal lobe involvement is not typical.

**(Choice C)** *Naegleria fowleri* is a free-living, protozoan parasite that causes rapid meningoencephalitis with a high mortality rate. *N fowleri* is found in fresh water, and transmission occurs through nasal inhalation during recreational activities (eg, swimming, diving). After spread through the cribriform plate to the olfactory cortex, infection leads to symptoms of encephalitis, as described above, in addition to smell and taste abnormalities. Inflammation can be seen in the frontal and temporal lobes, brainstem, and meninges.

**(Choices D and E)** *Neisseria meningitidis* and *Streptococcus pneumoniae* are the 2 most common causes of bacterial meningitis. Unlike encephalitis, meningitis does not affect the brain parenchyma; rather, infection of the connective tissue layers of the brain leads to classic symptoms of fever, nuchal rigidity, and


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by polymerase chain reaction testing of cerebrospinal fluid.

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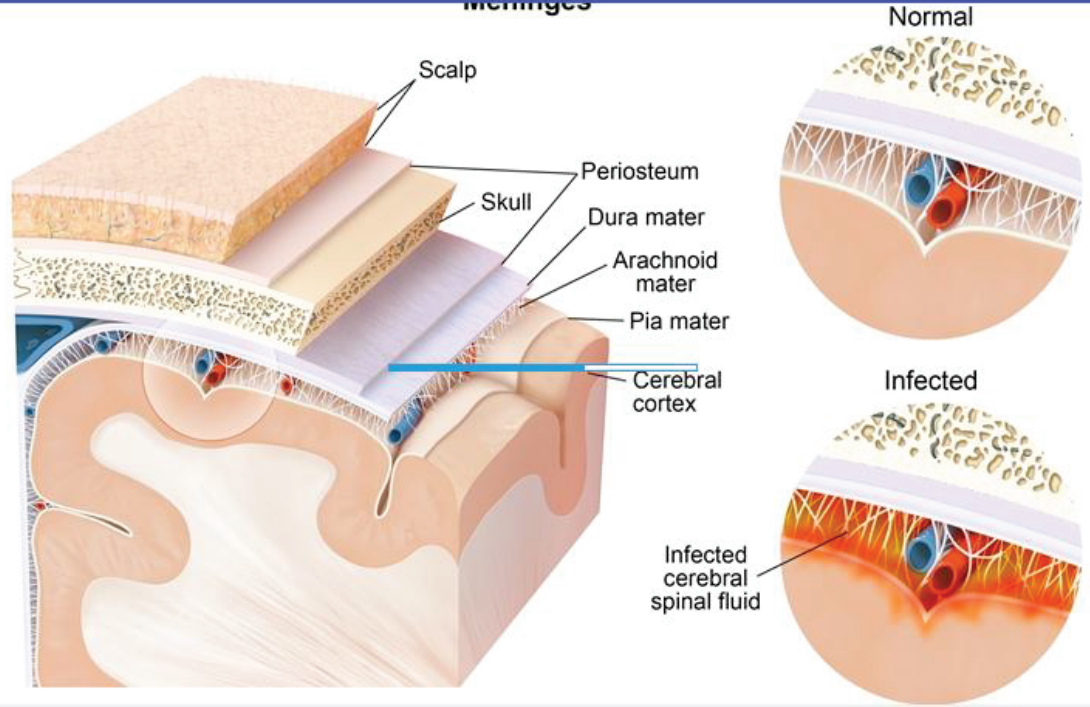


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altered mental status.

**(Choice F)** Immunocompromised hosts (eg, patients with HIV) are predisposed to opportunistic pathogens (eg, *Toxoplasma gondii*, cytomegalovirus [CMV]) that can cause encephalitis. Toxoplasma encephalitis is classically associated with ring-enhancing lesions (white arrows) in the parietal or frontal lobes after ingestion of oocysts from soil or cat litter. CMV encephalitis can lead to parenchymal micro-nodules and ventricular enlargement.

**Educational objective:**
Herpes simplex virus type 1 encephalitis is a potentially fatal complication from primary infection or reactivation of latent disease. Nervous system invasion leads to necrosis of the temporal lobe, which can result in aphasia and personality changes in addition to classic features of encephalitis (eg, headache, fever, altered mental status, seizure).

**References**

- Herpes simplex encephalitis: adolescents and adults.
- Herpes simplex encephalitis: from virus to therapy.

Microbiology Nervous System HSV infection



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www.ncbi.nlm.nih.gov/pubmed/21488834

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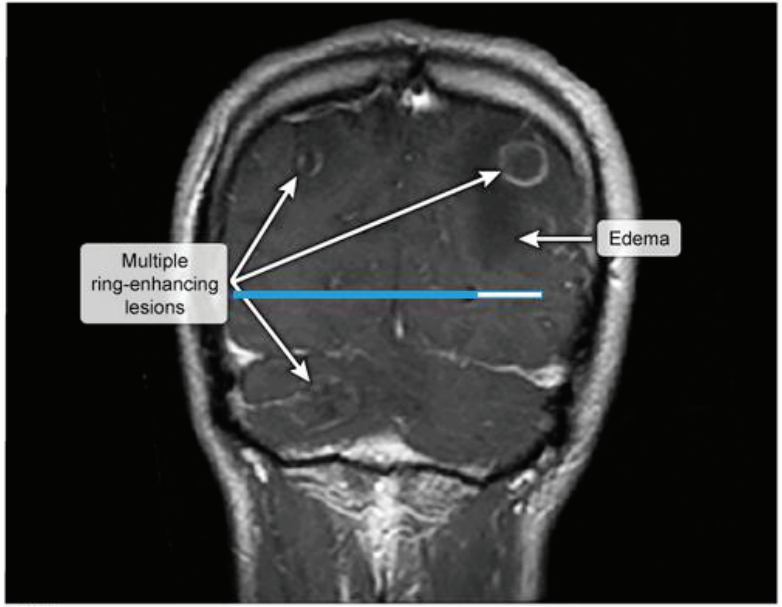
**Toxoplasma encephalitis**

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Microbiology | Nervous System | HSV infection



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A 35-year-old woman comes to the office due to trouble seeing out of her right eye. The patient started having blurry vision and pain with eye movement 2 days ago. She has no headache, vertigo, slurred speech, numbness, or weakness. Two years ago, the patient had an episode of double vision that spontaneously resolved after a few weeks. On physical examination, she has an afferent pupillary defect with markedly reduced visual acuity on the right. Funduscopy reveals blurring of the optic disk margins in the right eye. MRI of the brain reveals multiple, ovoid white matter lesions with perpendicular orientation to the lateral ventricles. This patient's condition is most likely caused by an inappropriate immune response directed against which of the following cells?

- A. Astrocytes
- B. Ependymal cells
- C. Microglial cells
- D. Oligodendrocytes
- E. Schwann cells



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having blurry vision and pain with eye movement 2 days ago. She has no headache, vertigo, slurred speech, numbness, or weakness. Two years ago, the patient had an episode of double vision that spontaneously resolved after a few weeks. On physical examination, she has an afferent pupillary defect with markedly reduced visual acuity on the right. Funduscopy reveals blurring of the optic disk margins in the right eye. MRI of the brain reveals multiple, ovoid white matter lesions with perpendicular orientation to the lateral ventricles. This patient's condition is most likely caused by an inappropriate immune response directed against which of the following cells?

A. Astrocytes (1%)
B. Ependymal cells (4%)
C. Microglial cells (1%)
D. Oligodendrocytes (87%)
E. Schwann cells (4%)

Correct

87%
52 secs
02/27/2021



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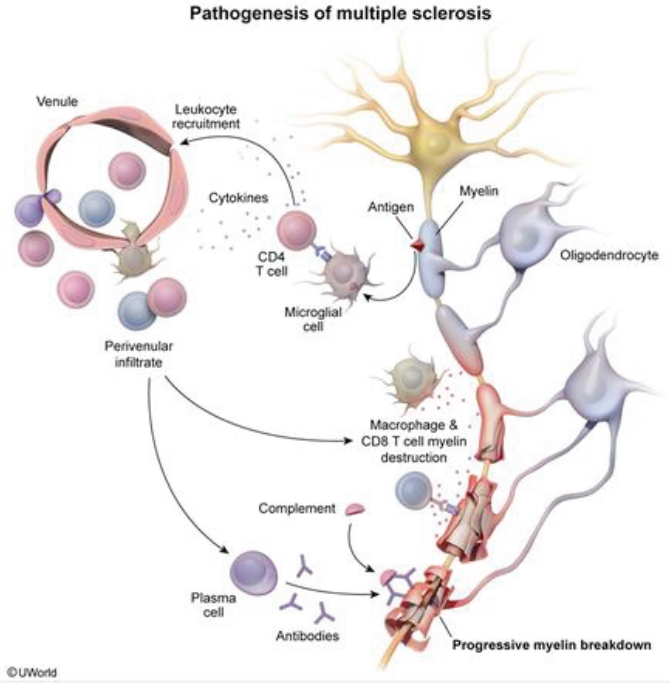


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This patient likely has **multiple sclerosis** (MS), an autoimmune demyelinating disease of the central nervous system (CNS) that typically presents in young women (age <50) with **neurologic deficits** (eg, blurry vision, diplopia, focal weakness/numbness, dysarthria, bowel/bladder dysfunction) **disseminated in time and space**. A common initial manifestation of MS is **optic neuritis**, characterized by monocular visual loss with pain on eye movement and an afferent pupillary defect. MRI findings in MS typically include white matter lesions scattered throughout the brain and/or spinal cord with a predilection for the subcortical periventricular regions.

The pathogenesis of MS involves an autoimmune response targeting **oligodendrocytes**, the myelin-producing cells of the CNS. Helper T cells abnormally react to antigens in myelin, causing a release of inflammatory cytokines (eg, interferon-gamma) that promote the infiltration of destructive macrophages/microglia and leukocytes. B cells also play a role as most patients with MS have oligoclonal immunoglobulin bands in the cerebrospinal fluid. Myelin degeneration leads to slowed nerve conduction with neurologic deficits as described above.

**(Choice A)** Astrocytes are glial cells (non-neural cells) that contribute to the blood-brain barrier and play an important role in potassium buffering, neurotransmitter metabolism, and glial scar formation. Astrocytes proliferate and form the scar (gliosis) after the attack on oligodendrocytes; astrocytes are usually not



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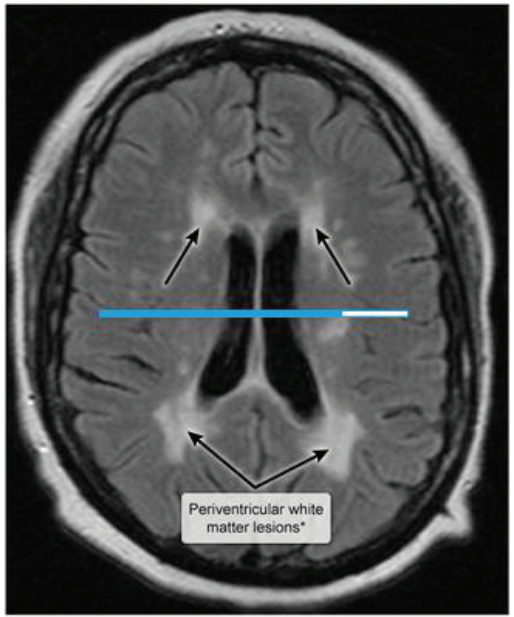
## Exhibit Display

**Multiple sclerosis**




*Demyelinating plaques

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proliferate and form the scar (gliosis) after the attack on oligodendrocytes; astrocytes are usually not



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proliferate and form the scar (gliosis) after the attack on oligodendrocytes; astrocytes are usually not targeted by the immunologic response in MS.

**(Choice B)** Ependymal cells are ciliated glial cells that line the ventricles of the brain and the central canal of the spinal cord. They also make up the choroid plexus and produce cerebrospinal fluid. These cells are not targeted by the immune response in MS.

**(Choice C)** Microglia function as the resident macrophages in the CNS. Although they participate in myelin destruction, they are not the target of the immune response in MS.

**(Choice E)** Schwann cells are the myelin-producing cells of the peripheral nervous system. These cells are targeted by the immunologic response associated with peripheral demyelinating disorders (eg, Guillain-Barré syndrome).

**Educational objective:**
The pathogenesis of multiple sclerosis involves an autoimmune response (T cell and antibody-mediated) targeting oligodendrocytes and myelin in the central nervous system, leading to slowed nerve conduction with neurologic deficits.

**References**

- Immunopathogenesis of multiple sclerosis


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A 31-year-old woman is brought to the hospital due to respiratory difficulty. She has had trouble performing her daily activities for the past few weeks due to fatigue. In particular, her arms seem to "just drop" when she combs her hair. The patient's symptoms are generally better in the morning and worsen throughout the day. She does not use tobacco, alcohol, or illicit drugs. Examination shows diplopia. Chest auscultation shows normal heart and breath sounds. Deep tendon reflexes are normal. Babinski sign is absent. The results of arterial blood gas analysis are as follows:

| | |
|---|---|
| pH | 7.32 |
| $pCO_2$ | 60 mm Hg |
| $pO_2$ | 60 mm Hg |

Which of the following is most likely abnormal in this patient?

A. Acetylcholine release from presynaptic neurons
B. Acetylcholinesterase activity
C. Calcium entry into presynaptic neurons


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shows normal heart and breath sounds. Deep tendon reflexes are normal. Babinski sign is absent. The results of arterial blood gas analysis are as follows:

| | |
|---|---|
| pH | 7.32 |
| $pCO_2$ | 60 mm Hg |
| $pO_2$ | 60 mm Hg |

Which of the following is most likely abnormal in this patient?

A. Acetylcholine release from presynaptic neurons
B. Acetylcholinesterase activity
C. Calcium entry into presynaptic neurons
D. Number of acetylcholine receptors
E. Reuptake of acetylcholine

Submit



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shows normal heart and breath sounds. Deep tendon reflexes are normal. Babinski sign is absent. The results of arterial blood gas analysis are as follows:

| | |
|---|---|
| pH | 7.32 |
| $pCO_2$ | 60 mm Hg |
| $pO_2$ | 60 mm Hg |

Which of the following is most likely abnormal in this patient?

A. ~~Acetylcholine release from presynaptic neurons~~ (10%)
B. ~~Acetylcholinesterase activity~~ (4%)
C. ~~Calcium entry into presynaptic neurons~~ (6%)
D. Number of acetylcholine receptors (76%)
E. Reuptake of acetylcholine (2%)

Correct

76%

01 min, 01 sec

01/24/2021



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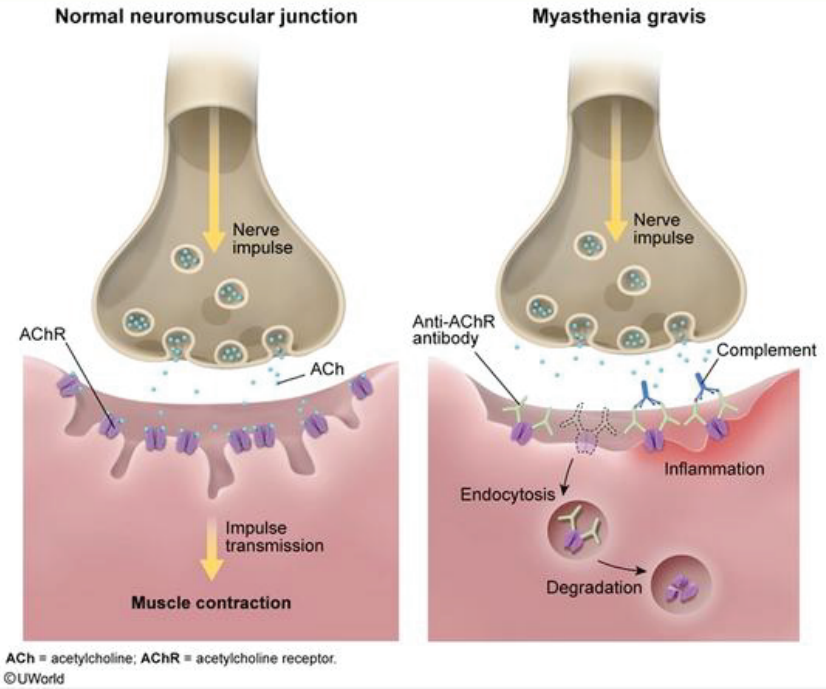


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**Myasthenia gravis** (MG) is an acquired autoimmune disorder characterized by fatigable, fluctuating weakness of the skeletal muscles. The most commonly affected muscles include **ocular** (diplopia, ptosis), bulbar (dysarthria, fatigable chewing), facial (loss of smile), and proximal (**neck/shoulder weakness**) muscles. However as the disease progresses, **respiratory failure** (↓ pH, ↑ $pCO_2$, ↓ $O_2$) can occur due to diaphragmatic weakness and patients may require intubation.

MG is caused by an autoantibody-mediated, T cell–dependent attack on the **acetylcholine receptors** (AChRs) of the **postsynaptic** neuromuscular junction. Antibody-mediated blockade of the active site of AChRs prevents acetylcholine from binding and triggers endocytosis of AChRs (receptor internalization) and complement-mediated postsynaptic membrane damage. Over time, these changes result in **reduced numbers of AChRs** and impaired neuromuscular transmission.

**(Choice A)** Botulinum toxin irreversibly blocks acetylcholine release from presynaptic membranes of neuromuscular junctions. After exposure to the toxin, patients may develop cranial nerve abnormalities (including ptosis and facial weakness), symmetric descending weakness, and respiratory failure. However, autonomic abnormalities are common, and symptoms are rapidly progressive (hours rather than weeks) and do not worsen with repetition.



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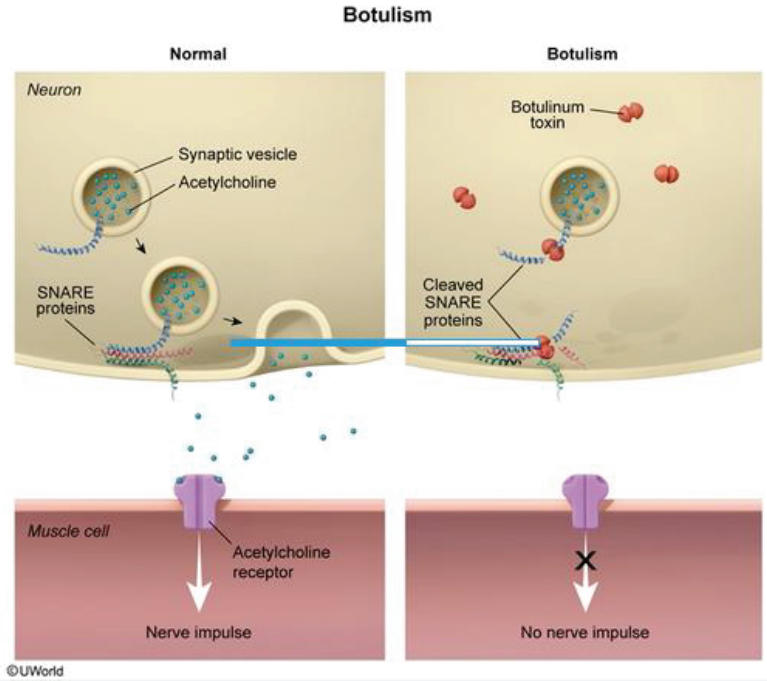


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autonomic abnormalities are common, and symptoms are rapidly progressive (hours rather than weeks) and do not worsen with repetition.

**(Choices B and E)** The action of acetylcholine at the postsynaptic membrane is terminated by acetylcholinesterase, not by acetylcholine reuptake. Organophosphates (eg, pesticides, sarin gas) irreversibly inactivate acetylcholinesterase, causing cholinergic toxicity (eg, increased glandular secretions, widespread smooth muscle activation). Muscle weakness, including respiratory failure, can occur due to depolarizing blockade at the neuromuscular junction; however, other symptoms (eg, diarrhea, urination, miosis, bradycardia, emesis, salivation) would be expected.

**(Choice C)** Lambert-Eaton myasthenic syndrome is due to autoantibodies directed against the voltage-gated calcium channels on presynaptic nerve terminals, leading to reduced calcium entry and impaired acetylcholine release. This syndrome commonly occurs in association with malignancy, particularly small cell lung cancer (which would be atypical in this young female), and generally causes proximal extremity weakness that is worse in the mornings and **improves** with repetition. Autonomic findings (eg, dry mouth, erectile dysfunction in males) are frequently seen and can be an important clue to diagnosis.

**Educational objective:**
Myasthenia gravis is an autoimmune disorder caused by an autoantibody-mediated attack on the


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depolarizing blockade at the neuromuscular junction; however, other symptoms (eg, diarrhea, urination, miosis, bradycardia, emesis, salivation) would be expected.

**(Choice C)** Lambert-Eaton myasthenic syndrome is due to autoantibodies directed against the voltage-gated calcium channels on presynaptic nerve terminals, leading to reduced calcium entry and impaired acetylcholine release. This syndrome commonly occurs in association with malignancy, particularly small cell lung cancer (which would be atypical in this young female), and generally causes proximal extremity weakness that is worse in the mornings and **improves** with repetition. Autonomic findings (eg, dry mouth, erectile dysfunction in males) are frequently seen and can be an important clue to diagnosis.

**Educational objective:**
Myasthenia gravis is an autoimmune disorder caused by an autoantibody-mediated attack on the acetylcholine receptors of the postsynaptic neuromuscular junction, leading to a reduced number of acetylcholine receptors. It is characterized by fatigable weakness of the skeletal muscles; respiratory failure can occur due to diaphragmatic weakness.

| Pathology | Nervous System | Myasthenia gravis |
|---|---|---|
| Subject | System | Topic |


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A 63-year-old man collapses at home after experiencing severe retrosternal chest pain. The emergency medical team finds him with no pulse, and cardiac monitoring shows ventricular fibrillation. Cardiopulmonary resuscitation is performed, and the patient regains spontaneous circulation after several minutes. On arrival at the hospital, he has stable vital signs but does not follow commands or respond to strong stimuli. Which of the following areas is most likely to be affected first by ischemic damage in this patient?

A. Caudate nucleus
B. Hippocampus
C. Hypothalamus
D. Substantia nigra
E. Thalamic nuclei

Submit



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A 63-year-old man collapses at home after experiencing severe retrosternal chest pain. The emergency medical team finds him with no pulse, and cardiac monitoring shows ventricular fibrillation. Cardiopulmonary resuscitation is performed, and the patient regains spontaneous circulation after several minutes. On arrival at the hospital, he has stable vital signs but does not follow commands or respond to strong stimuli. Which of the following areas is most likely to be affected first by ischemic damage in this patient?

- A. Caudate nucleus (5%)
- ✓ B. Hippocampus (64%)
- C. Hypothalamus (5%)
- D. Substantia nigra (1%)
- E. Thalamic nuclei (23%)

Correct

64% Answered correctly

12 secs Time Spent

03/21/2021 Last Updated



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This patient's cardiac arrest, secondary to ventricular fibrillation, caused rapid cessation of cerebral blood flow and **global cerebral ischemia**. Although cardiac function and circulation were restored after medical intervention, the patient's brain was subjected to ischemia for an unknown length of time, resulting in neurological impairment.

Global ischemia lasting longer than 3-5 minutes can cause irreversible damage to neurons. The cells that are typically **affected first** by hypoxia are the CA1 pyramidal neurons of the **hippocampus**, which can be damaged by ischemia in as little as 3 minutes. The cerebellar Purkinje cells and neocortex pyramidal neurons are also highly susceptible to damage if ischemia lasts for 5-10 minutes. These neurons are likely vulnerable to ischemia because of their **high metabolic demand** and unique neurochemical characteristics (eg, inability to repolarize after anoxic depolarization).

The hippocampus is located in the medial temporal lobe and plays an essential role in memory, spatial processing, and response inhibition. Selective damage to the hippocampus is common with transient ischemia and can result in an inability to make new memories (anterograde amnesia) and disorientation to place or time.

**(Choices A, C, D, and E)** Although the caudate nucleus, hypothalamus, substantia nigra, and thalamic nuclei are also vulnerable to ischemia if cerebral hypoxia is sustained, they are not as susceptible to


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The hippocampus is located in the medial temporal lobe and plays an essential role in memory, spatial processing, and response inhibition. Selective damage to the hippocampus is common with transient ischemia and can result in an inability to make new memories (anterograde amnesia) and disorientation to place or time.

**(Choices A, C, D, and E)** Although the caudate nucleus, hypothalamus, substantia nigra, and thalamic nuclei are also vulnerable to ischemia if cerebral hypoxia is sustained, they are not as susceptible to damage as the hippocampal CA1 pyramidal neurons.

**Educational objective:**

Global cerebral ischemia is typically precipitated by systemic hypotension (eg, cardiac arrest). The cells most susceptible to ischemia are the CA1 pyramidal neurons of the hippocampus. Other areas of the brain that are damaged early in the course of global cerebral ischemia include the cerebellar Purkinje cells and the pyramidal neurons of the neocortex.

**References**


- Mechanisms of injury in hypoxic-ischemic encephalopathy: implications to therapy.
- Mechanisms of brain injury after global cerebral ischemia.




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www.ncbi.nlm.nih.gov/pubmed/16443127

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A 65-year-old man is brought to the emergency department due to acute-onset, right-sided weakness and slurred speech. He also has a severe headache and nausea. Medical history is significant for poorly controlled hypertension and chronic tobacco use. Blood pressure is 240/120 mm Hg and pulse is 104/min. On physical examination, the patient is lethargic with right hemiparesis and lower facial weakness, right hemisensory loss, and dysarthria. Noncontrast CT scan of the head is shown in the image below.

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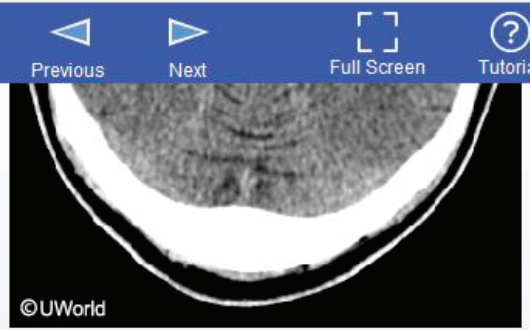


Which of the following cerebral blood vessels is most likely affected in this patient?

- A. Cortical branches
- B. Inferior division of middle cerebral artery
- C. Lenticulostriate arteries
- D. Pontine arteries
- E. Posterior cerebral artery
- F. Superior division of middle cerebral artery

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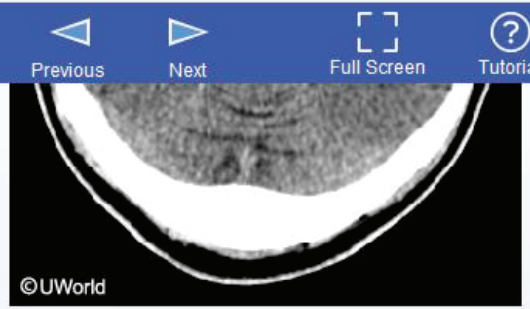


Which of the following cerebral blood vessels is most likely affected in this patient?

A. ~~Cortical branches~~ (1%)

B. Inferior division of middle cerebral artery (19%)

C. Lenticulostriate arteries (59%)

D. ~~Pontine arteries~~ (2%)

E. ~~Posterior cerebral artery~~ (1%)

F. Superior division of middle cerebral artery (15%)

Incorrect
Correct answer

59%

01 min, 12 secs

01/03/2021



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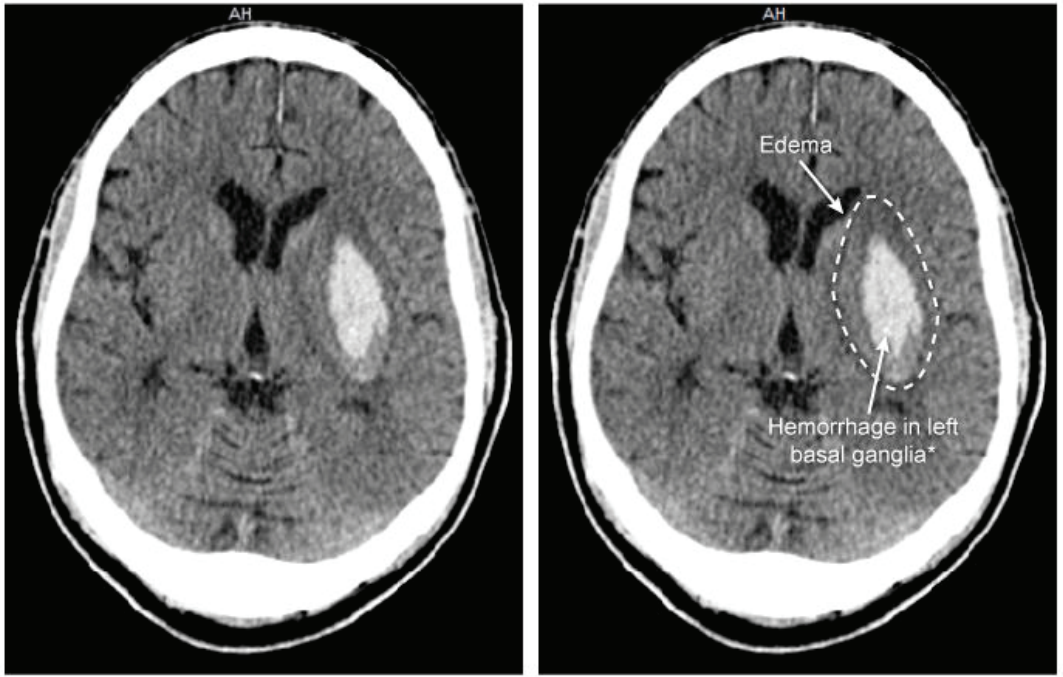
## Putamen hemorrhage




*Putamen and globus pallidus hemorrhage: usually due to uncontrolled hypertension

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This patient's CT findings (eg, hyperdense mass) are consistent with an acute **putaminal hemorrhage** (ie, affecting the basal ganglia). Because of their location, putaminal hemorrhages almost always affect the adjacent **internal capsule**, leading to **dysarthria**, contralateral **hemiparesis**, and contralateral **hemisensory loss** due to disruption of the corticobulbar, corticospinal, and somatosensory fibers. As the hemorrhage expands, it leads to increase intracranial pressure (headache, nausea/vomiting, and altered mental status), midline shift from mass effect, and possible cerebral herniation.

**Hypertensive vasculopathy** involving the small, penetrating branches of the major cerebral arteries is the most common cause of spontaneous deep intracerebral hemorrhage. Chronic hypertension leads to the formation of Charcot-Bouchard aneurysms, which may ultimately rupture and bleed within the deep brain structures. The most frequently affected locations include the basal ganglia (putamen), cerebellar nuclei, and pons. The basal ganglia are supplied by the **lenticulostriate arteries**, which are deep, small vessel branches off the middle cerebral arteries.

**(Choice A)** Cortical branches of the major cerebral arteries are affected in lobar hemorrhages (eg, occipital), as opposed to deep hypertensive hemorrhages. Spontaneous lobar hemorrhages tend to occur in the elderly due to amyloid angiopathy.

**(Choices B, E, and F)** The middle (inferior and superior divisions) and posterior cerebral arteries are



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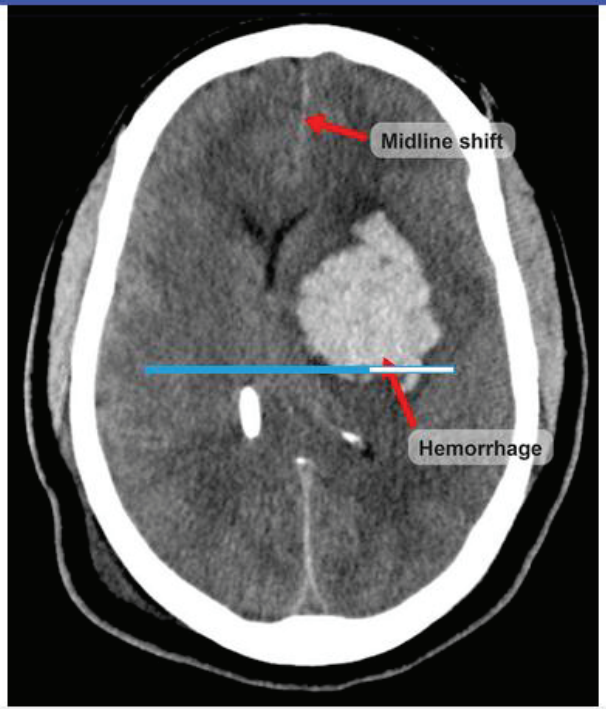


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(Choices B, E, and F) The middle (inferior and superior divisions) and posterior cerebral arteries are



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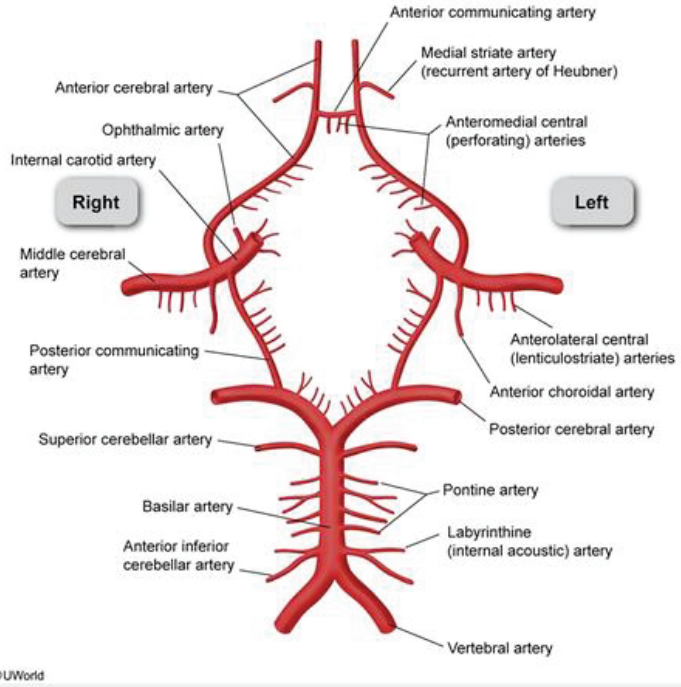


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(Choices B, E, and F) The middle (inferior and superior divisions) and posterior cerebral arteries are



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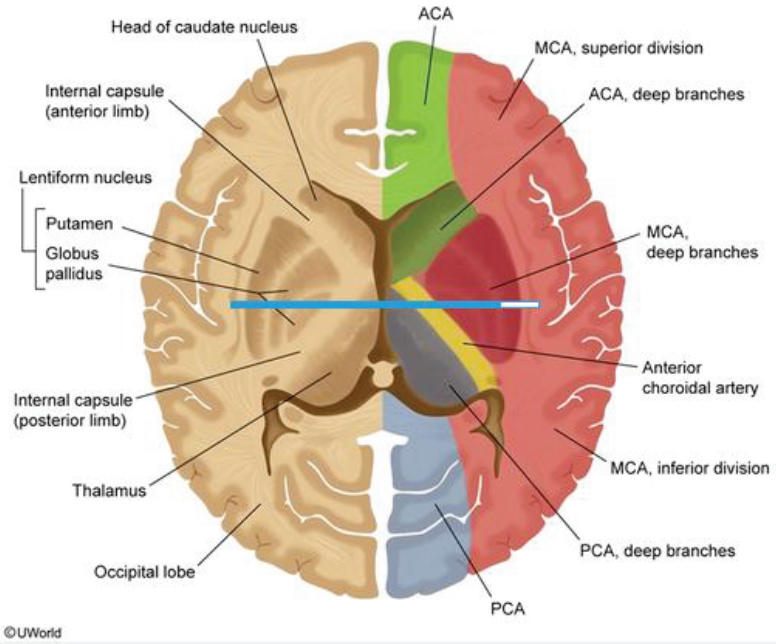
Blood supply to the cerebral hemispheres

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(Choices B, E, and F) The middle (inferior and superior divisions) and posterior cerebral arteries are



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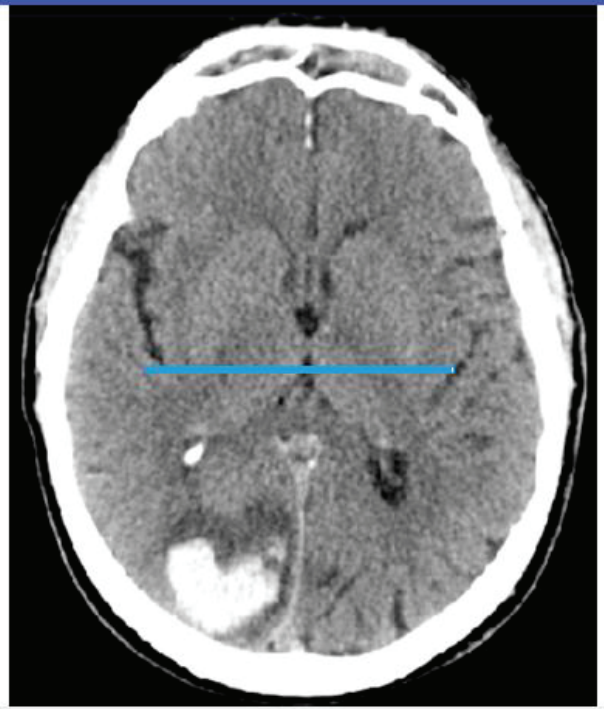

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(Choices B, E, and F) The middle (inferior and superior divisions) and posterior cerebral arteries are



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**(Choices B, E, and F)** The middle (inferior and superior divisions) and posterior cerebral arteries are large, proximal vessels arising from the circle of Willis. These arteries are typically associated with ischemic stroke due to thrombotic/embolic vessel occlusion or subarachnoid hemorrhage after saccular aneurysm rupture; intracerebral hemorrhage involving the basal ganglia is more likely due to rupture of deep penetrating arteries.

**(Choice D)** The pontine arteries are small branches of the basilar artery that can rupture in the setting of poorly controlled chronic hypertension. Pontine hemorrhages usually occur close to the midline and affect both sides of the pons. They typically present with coma (disruption of the reticular activating system), locked-in syndrome (corticospinal and corticobulbar tracts), and pinpoint pupils (descending sympathetic tract).

**Educational objective:**

Spontaneous deep intracerebral hemorrhage is typically caused by hypertensive vasculopathy involving the small, penetrating branches of the major cerebral arteries. The most frequently affected locations include the basal ganglia (putamen), cerebellar nuclei, thalamus, and pons. The putamen is supplied by the lenticulostriate arteries, which are deep, small vessel branches off the middle cerebral arteries.

**References**



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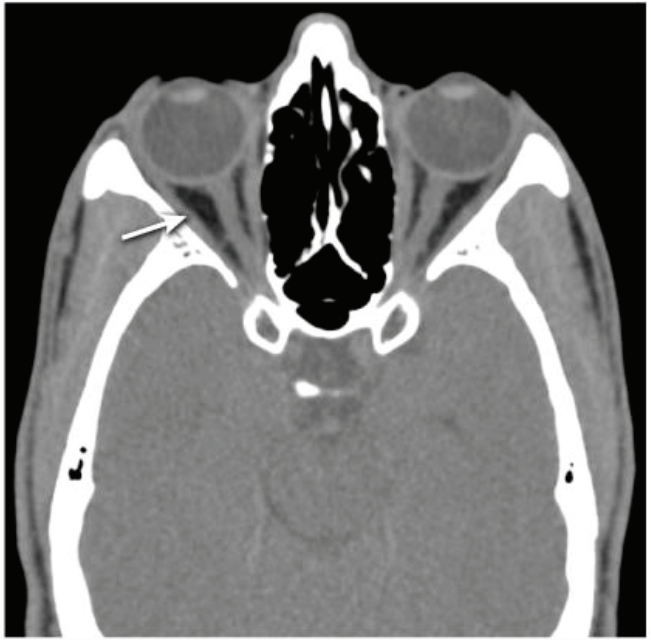
A 32-year-old woman comes to the office due to a 2-day history of worsening headache and double vision. The patient reports no chronic medical conditions but has had nasal discharge for the past several days. Physical examination shows weakness of the muscle shown on the below CT scan:





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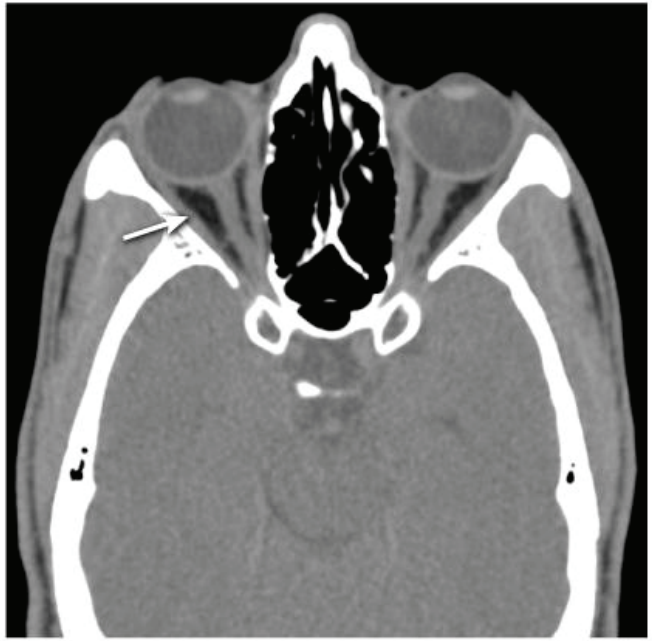

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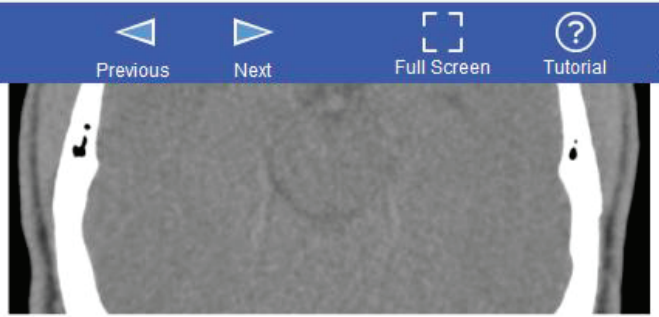

Purulent discharge from the sphenoethmoidal recess of the nasal cavity is also noted. Involvement of which of the following nerves best explains this patient's ocular findings?

A. Optic nerve
B. Oculomotor nerve
C. Trochlear nerve
D. Ophthalmic division of the trigeminal nerve
E. Abducens nerve

Submit



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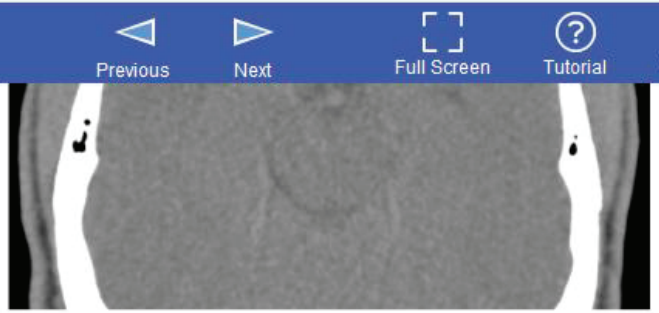

Purulent discharge from the sphenoethmoidal recess of the nasal cavity is also noted. Involvement of which of the following nerves best explains this patient's ocular findings?

- A. Optic nerve (4%)
- B. Oculomotor nerve (9%)
- C. Trochlear nerve (6%)
- D. Ophthalmic division of the trigeminal nerve (3%)
- ✓ E. Abducens nerve (75%)

Correct

75%

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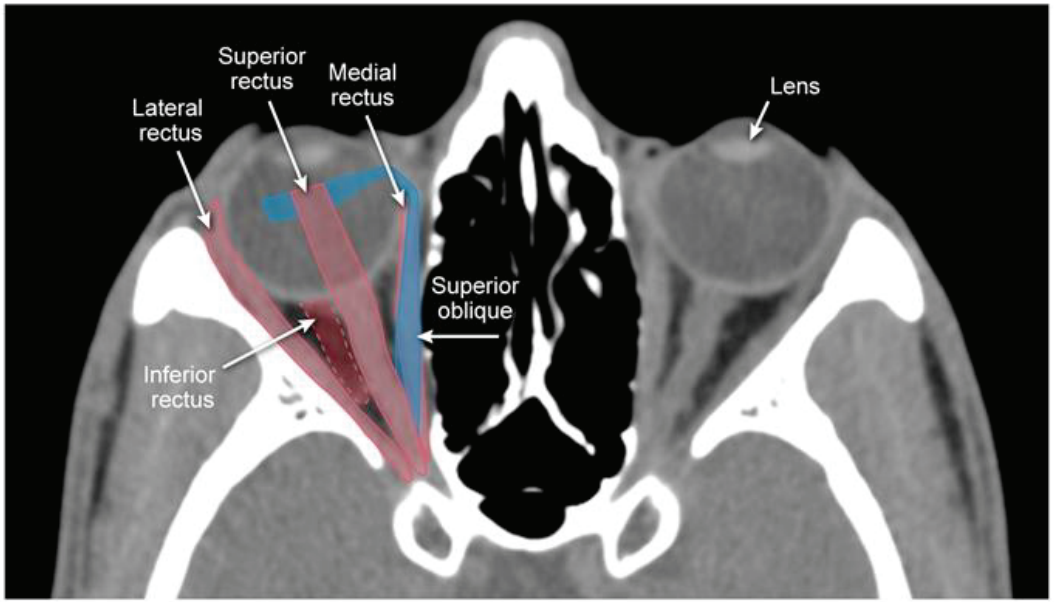
## Extraocular muscles on CT scan

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The arrow in the above CT scan points to an extraocular muscle that originates at the annular tendon and inserts onto the **temporal (ie, lateral) surface of the globe**. The extraocular muscles control movement of



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The arrow in the above CT scan points to an extraocular muscle that originates at the annular tendon and inserts onto the **temporal (ie, lateral) surface of the globe**. The extraocular muscles control movement of the globe; dysfunction leads to double vision. They are innervated by the following:

- The oculomotor nerve (CN III) innervates the superior rectus, medial rectus, inferior rectus, inferior oblique, and levator palpebrae superioris. It also contributes parasympathetic innervation to the ciliary muscle and iris sphincter for the efferent path of the pupillary reflex **(Choice B)**.
- The trochlear nerve (CN IV) innervates only the superior oblique muscle, which causes the eye to intort (internally rotate) and depress while adducted **(Choice C)**.
- The **abducens nerve (CN VI)** innervates the **lateral rectus muscle**, which **abducts the eye**.

**Acute sinusitis** can have significant complications, including **cavernous sinus thrombosis** due to contiguous spread of an infection through the valveless facial venous system. This can cause dysfunction of nerves that travel through the cavernous sinus, including those that innervate the extraocular muscles.

**(Choice A)** The optic nerve (CN II) transmits visual information to the brain; damage to this nerve causes loss of vision. The optic nerve has no role in movement of the globe.



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- The **abducens**

**Acute sinusitis** ca
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**(Choice A)** The op
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| Nerve | Eye muscle(s) innervated | Oculomotor functions | Lesion findings |
|---|---|---|---|
| **Oculomotor (CN III)** | • Superior rectus<br>• Medial rectus<br>• Inferior rectus<br>• Inferior oblique<br>• Levator palpebrae superioris | • Adduction<br>• Depression<br>• Elevation<br>• External rotation | • Eye deviated downward & laterally<br>• Diagonal diplopia<br>• Dilation of pupil & loss of accommodation<br>• Ptosis |
| **Trochlear (CN IV)** | • Superior oblique | • Abduction<br>• Internal rotation<br>• Depression while adducted | • Eye deviated upward<br>• Vertical & torsional diplopia |
| **Abducens (CN VI)** | • Lateral rectus | • Abduction | • Eye deviated medially<br>• Horizontal diplopia |

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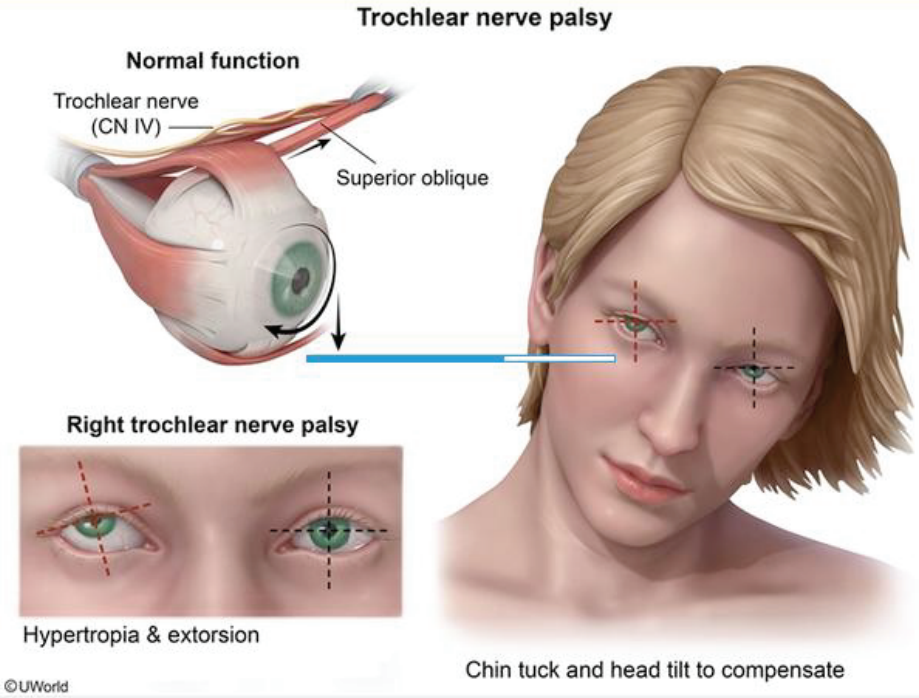


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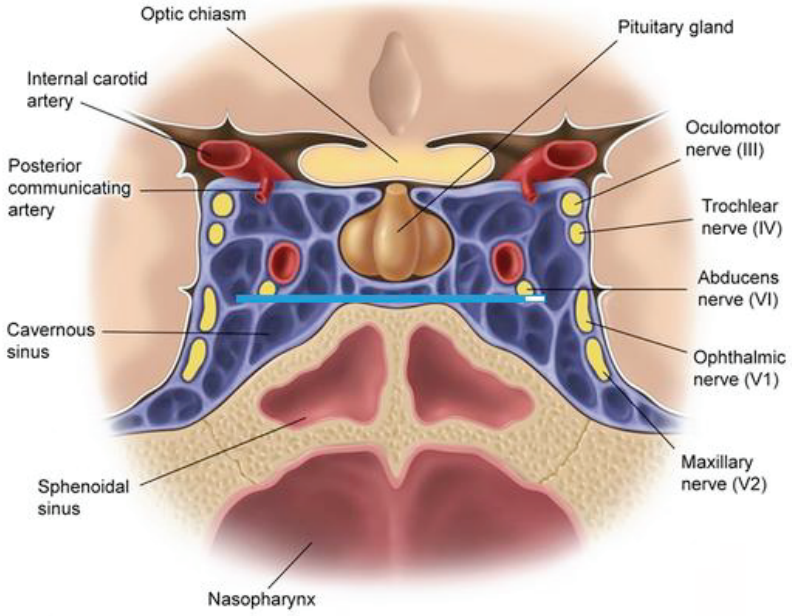
Cavernous sinus

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The abducens nerve (CN VI) innervates the lateral rectus muscle, which abducts the eye.

**Acute sinusitis** can have significant complications, including **cavernous sinus thrombosis** due to contiguous spread of an infection through the valveless facial venous system. This can cause dysfunction of nerves that travel through the cavernous sinus, including those that innervate the extraocular muscles.

**(Choice A)** The optic nerve (CN II) transmits visual information to the brain; damage to this nerve causes loss of vision. The optic nerve has no role in movement of the globe.

**(Choice D)** The ophthalmic division of the trigeminal nerve (CN V) conveys sensory information from the forehead, side of the nose, periorbital area, and cornea. It does not contribute motor innervation to the extraocular muscles.

**Educational objective:**
The abducens nerve (CN VI) innervates the lateral rectus muscle, which originates at the annular tendon and inserts on the temporal (ie, lateral) surface of the globe. It functions to abduct the eye.

| Anatomy | Nervous System | Cavernous sinus thrombosis |
|---|---|---|
| Subject | System | Topic |

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The **abducens nerve (CN VI)** innervates the **lateral rectus muscle**, which **abducts the eye**.

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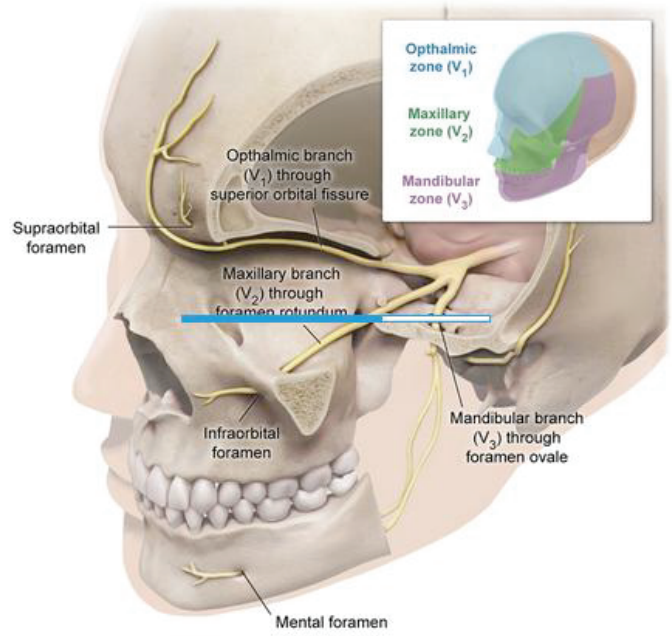
Trigeminal nerve distribution

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A 65-year-old Caucasian male presents to your office with increasing muscle rigidity and gait instability. He was diagnosed with Parkinson disease two years ago and has been treated with selegiline. His past medical history is otherwise insignificant. His father suffered from Parkinson disease and his mother died of an extensive stroke. You consider switching to levodopa to control this patient's symptoms adequately and discuss the adverse effect profile of levodopa with him. Which of the following adverse effects is most likely to persist after adding carbidopa to levodopa treatment?

A. Nausea and vomiting
B. Tachyarrhythmias
C. Hot flashes
D. Postural hypotension
E. Anxiety and agitation

Submit



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A 65-year-old Caucasian male presents to your office with increasing muscle rigidity and gait instability. He was diagnosed with Parkinson disease two years ago and has been treated with selegiline. His past medical history is otherwise insignificant. His father suffered from Parkinson disease and his mother died of an extensive stroke. You consider switching to levodopa to control this patient's symptoms adequately and discuss the adverse effect profile of levodopa with him. Which of the following adverse effects is most likely to persist after adding carbidopa to levodopa treatment?

- A. Nausea and vomiting (20%)
- B. Tachyarrhythmias (12%)
- C. Hot flashes (5%)
- D. Postural hypotension (16%)
- ✓ E. Anxiety and agitation (44%)

Correct

44% Answered correctly

59 secs Time Spent

01/30/2021 Last Updated



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Anxiety and agitation are central effects of dopamine and are caused by L-dopa, regardless of whether carbidopa is added to levodopa treatment. In fact, anxiety and agitation can be increased because more dopamine is available to the brain. (Adding carbidopa inhibits the peripheral conversion of levodopa, making more of it available to the brain.) High-dose combination levodopa/carbidopa can cause various behavioral changes such as anxiety, agitation, insomnia, confusion, delusions, and hallucinations. Reducing the dose is helpful in alleviating these adverse effects. If reduced dosage is not possible, atypical antipsychotics, such as clozapine, may be helpful.

**(Choice A)** Nausea and vomiting are seen in up to 80% of patients when levodopa is used alone. Dopamine stimulates the emetic center located in the brainstem (which is outside of the blood brain barrier). Adding a dopa decarboxylase inhibitor reduces nausea and vomiting and significantly increases patient compliance. Most patients develop tolerance to nausea after several months.

**(Choice B)** Tachyarrhythmias, such as ventricular extrasystoles and atrial fibrillation, are attributed to the increased peripheral formation of catecholamines. Adding a peripheral decarboxylase inhibitor reduces these arrhythmias.

**(Choices C and D)** Postural hypotension and hot flashes also result from the peripheral conversion of levodopa to dopamine, so a peripheral decarboxylase inhibitor would decrease these problems.


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**(Choice A)** Nausea and vomiting are seen in up to 80% of patients when levodopa is used alone. Dopamine stimulates the emetic center located in the brainstem (which is outside of the blood brain barrier). Adding a dopa decarboxylase inhibitor reduces nausea and vomiting and significantly increases patient compliance. Most patients develop tolerance to nausea after several months.

**(Choice B)** Tachyarrhythmias, such as ventricular extrasystoles and atrial fibrillation, are attributed to the increased peripheral formation of catecholamines. Adding a peripheral decarboxylase inhibitor reduces these arrhythmias.

**(Choices C and D)** Postural hypotension and hot flashes also result from the peripheral conversion of levodopa to dopamine, so a peripheral decarboxylase inhibitor would decrease these problems.

**Educational Objective:**
Adding carbidopa can reduce most of the peripheral side effects of levodopa. However, behavioral changes from levodopa can actually worsen with addition of carbidopa because more dopamine becomes available to the brain.

| Pharmacology | Nervous System | Parkinson disease |
|---|---|---|
| Subject | System | Topic |

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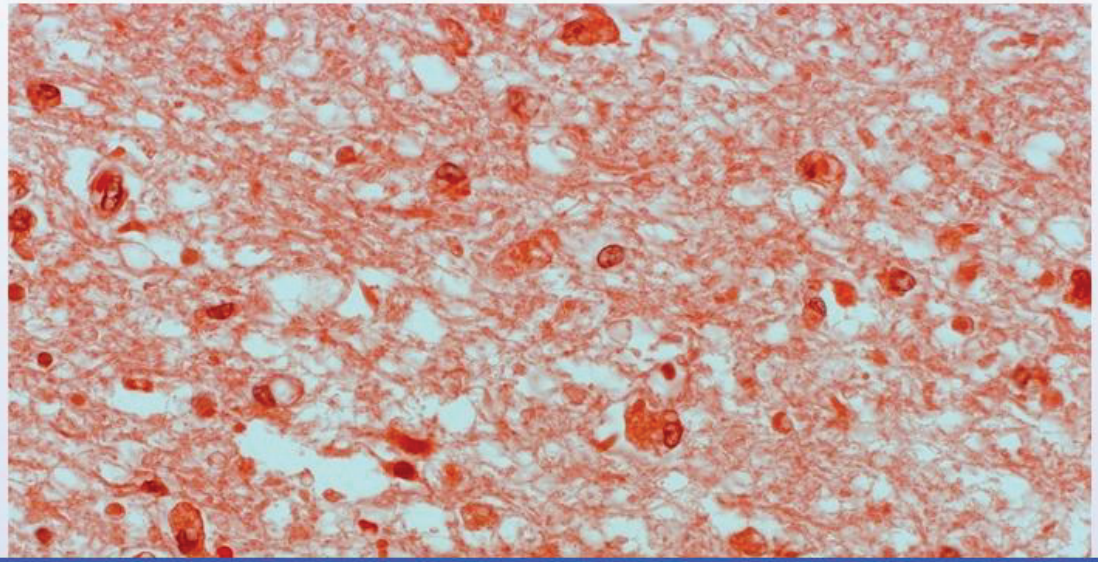
A 56-year-old man dies in the hospital due to aspiration-related complications. The patient was admitted 5 days ago with right-sided weakness, sensory loss, and difficulty with speech and swallowing. CT scan revealed an area of hypodensity in the left frontoparietal region. Autopsy examination is performed, and a section of loose, spongy tissue from the abnormal brain area is obtained. Histologic findings after staining for lipids are shown below.





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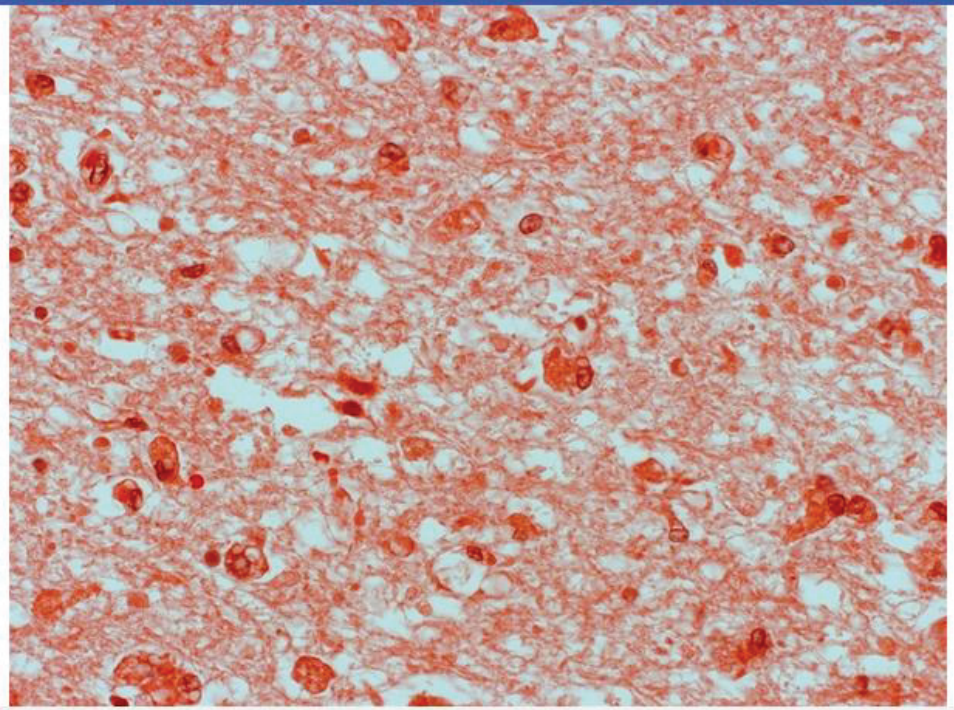

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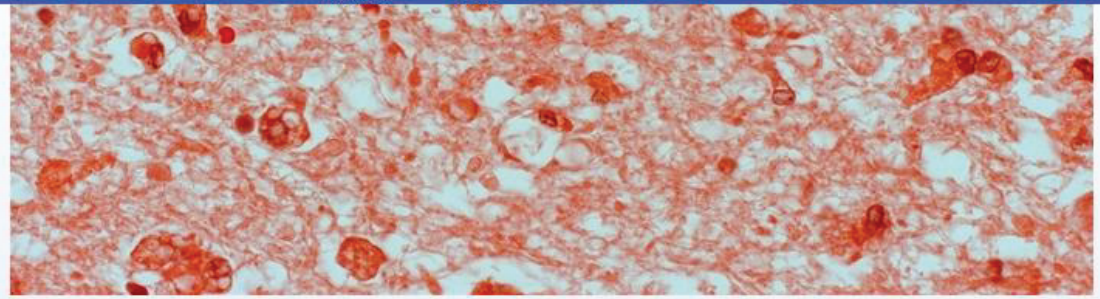

The cells most intensely stained in this patient's brain specimen represent which of the following cell types?

A. Astrocytes
B. Ependymal cells
C. Fibroblasts
D. Microglial cells
E. Neutrophils
F. Schwann cells



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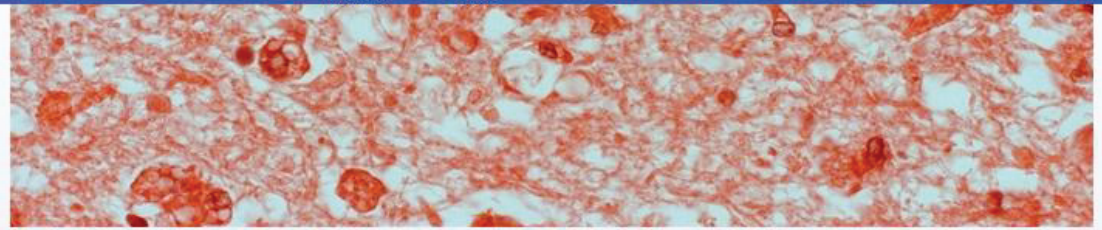

The cells most intensely stained in this patient's brain specimen represent which of the following cell types?

A. Astrocytes (25%)
B. Ependymal cells (3%)
C. Fibroblasts (1%)
D. Microglial cells (61%)
E. Neutrophils (3%)
F. Schwann cells (5%)

Correct

61%

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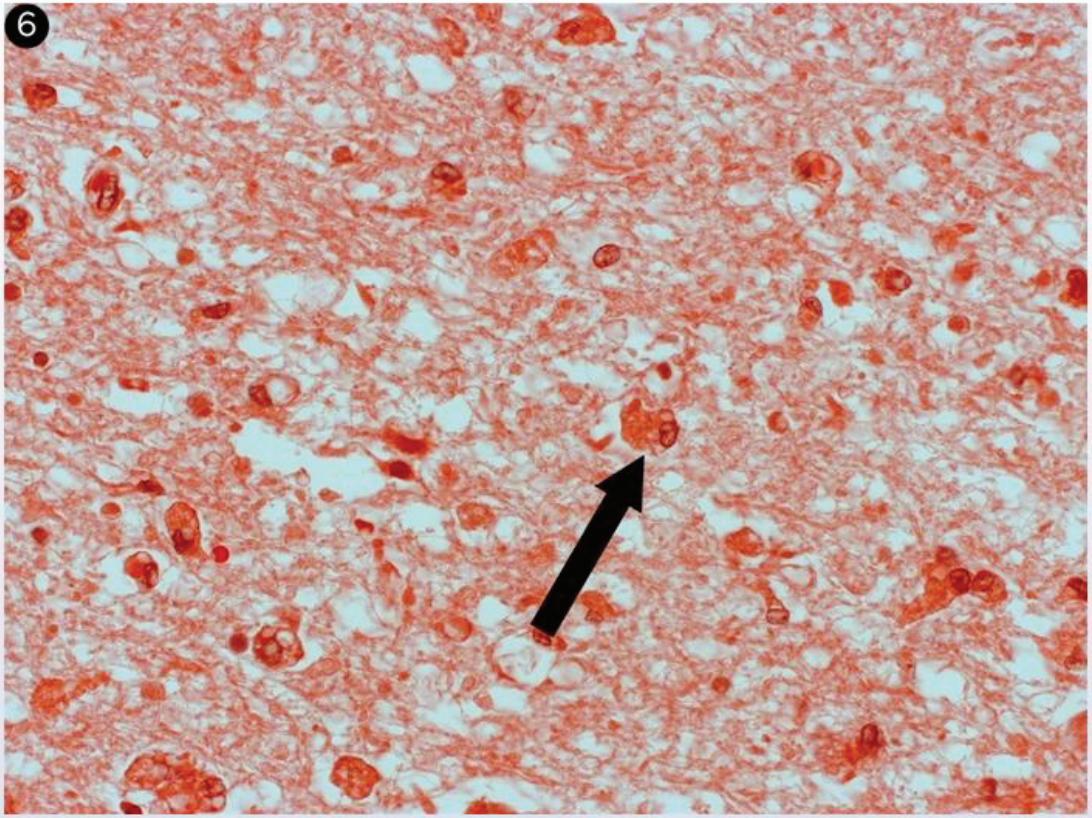



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This patient developed acute-onset neurologic defects (eg, hemiparesis, dysphagia, dysarthria) secondary to an ischemic stroke, which was confirmed by CT scan and autopsy findings. An **ischemic infarct** results from regional hypoperfusion (eg, thrombosis, embolism) or a global decline in cerebral blood flow. Characteristic CT findings are evident 6-12 hours after the onset of ischemic injury and include hypoattenuation of the tissue and loss of grey-white matter differentiation within the affected region.

Microscopically, neurons in the necrotic area display signs of irreversible damage during the first 24 hours after injury (red neurons). Neutrophils initially move into the area in the first 1-2 days, followed by **microglia** (derived from yolk-sac monocytes) 3-7 days after the onset of ischemia. As the neurons disintegrate, their fragments are phagocytized by microglia, and myelin breakdown products **accumulate** in the cytoplasm of microglia as **foamy lipids**. Infiltration of the brain tissue by microglia (arrow) is seen on light microscopy in the photo and is consistent with the expected histology findings 5 days post-infarction.

**(Choices A and C)** In peripheral tissues, fibroblasts migrate to the area of injury to participate in tissue repair. However, in the central nervous system, repair is instead performed by astrocytes that migrate to the area of necrosis within 2 weeks of injury to begin forming a glial scar.

**(Choices B and F)** Although both ependymal cells and Schwann cells process lipids and would be prominent on lipid stain, neither type of cell participates in central nervous system repair after ischemic



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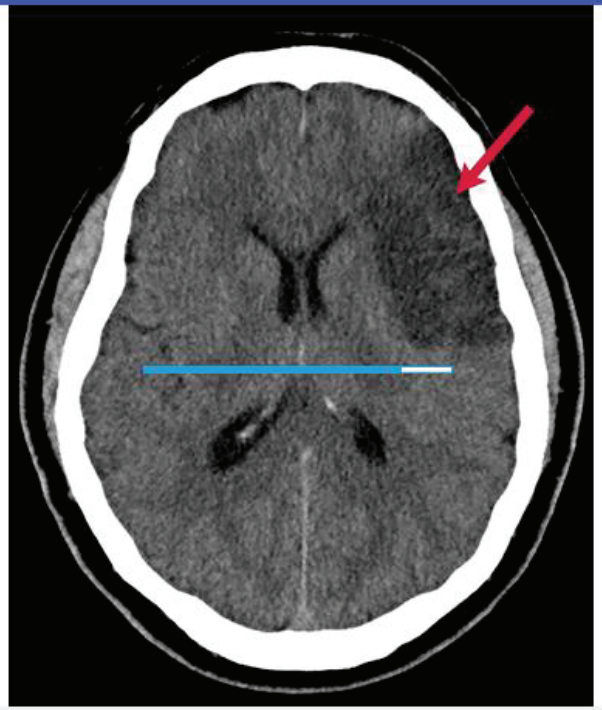

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prominent on lipid stain, neither type of cell participates in central nervous system repair after ischemic



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| Ischemic stroke | | |
|---|---|---|
| **Time after injury** | **Microscopic changes** | **Macroscopic changes** |
| 12-24 hours | Red neurons (eosinophilic cytoplasm, pyknotic nuclei, loss of Nissl substance) | |
| 24-72 hours | Neutrophilic infiltration | |
| 3-7 days | Macrophage/microglia infiltration & phagocytosis begins | |
| 1-2 weeks | Reactive gliosis & vascular proliferation around the necrotic area | Liquefactive necrosis (1 week-1 month) |
| >2 weeks | Glial scar formation | Cystic area surrounded by dense glial fibers (>1 month) |

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**(Choices A and C)**
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**(Choices A and C)** In peripheral tissues, fibroblasts migrate to the area of injury to participate in tissue repair. However, in the central nervous system, repair is instead performed by astrocytes that migrate to the area of necrosis within 2 weeks of injury to begin forming a glial scar.

**(Choices B and F)** Although both ependymal cells and Schwann cells process lipids and would be prominent on lipid stain, neither type of cell participates in central nervous system repair after ischemic infarction.

**(Choice E)** Neutrophils are the predominant type of inflammatory cell 1-2 days after cerebral infarction and release inflammatory mediators that contribute to the hydrolysis of cells in liquefactive necrosis. They would not be prominent on lipid stain.

**Educational objective:**
Microglia are the predominant cell in the necrotic area 3-7 days after the onset of ischemia and phagocytize the fragments of neurons, myelin, and necrotic debris.

| Pathology | Nervous System | Ischemic stroke |
|---|---|---|
| Subject | System | Topic |

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A 4-year-old boy is brought to the emergency department with dehydration. He has had several days of decreased oral intake, and today his parents could not get him to drink anything. The patient has received no vaccinations due to parental beliefs. Vital signs are normal except for mild tachycardia. Physical examination shows decreased skin turgor and sunken eyes. His jaw muscles are tight. Neurologic examination shows increased tone throughout and 3+ patellar reflexes. There is a small, healed puncture wound on his lower leg. The father says that the boy fell on a piece of chain-link fence in their backyard last week. Release of which of the following neurotransmitters is most likely to be directly impaired in this patient?

A. Acetylcholine
B. Dopamine
C. Glutamate
D. Glycine
E. Serotonin


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- A. Acetylcholine (28%)
- B. Dopamine (1%)
- C. Glutamate (13%)
- ✓ D. Glycine (56%)
- E. Serotonin (0%)

Correct

56%

01 min, 04 secs

11/27/2020



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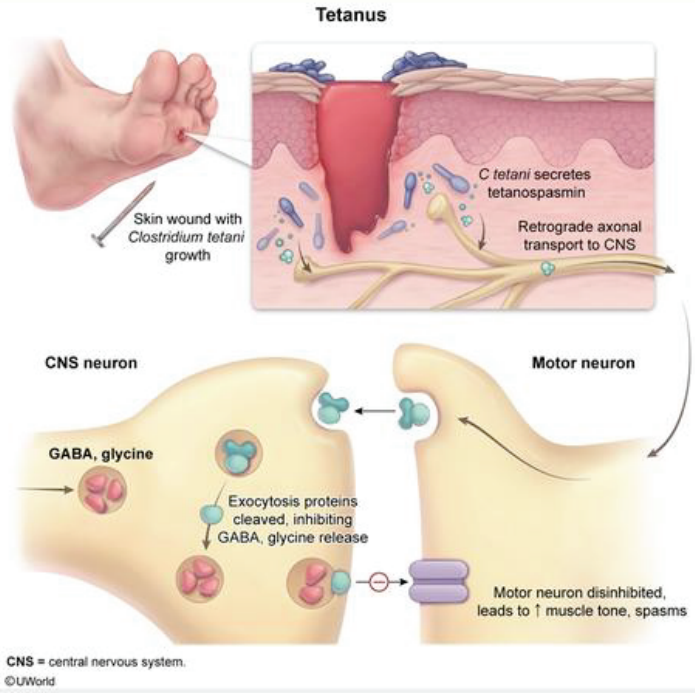


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This unvaccinated child has evidence of **tetanus** (*Clostridium tetani* infection) following a puncture wound. *C tetani* causes disease not through tissue invasion but by producing a potent metalloprotease **exotoxin** (tetanospasmin) that is deadly in nanogram quantities. The toxin first binds to receptors on the presynaptic membranes of peripheral motor neurons. From there, it migrates by **retrograde axonal transport** to central inhibitory neurons in the spinal cord and brain stem and prevents release of the inhibitory neurotransmitters **glycine** and **gamma-aminobutyric acid (GABA)**. Suppression of inhibitory nerve activity results in **increased activation** of motor nerves, causing **muscle spasms** and **hyperreflexia**. Classic features include difficulty opening the jaw (lockjaw, or **trismus**), a fixed sardonic smile (risus sardonicus), and contractions of back muscles resulting in backward arching (**opisthotonos**). Patients are also extremely irritable and develop tetanic spasms in response to minor stimuli such as loud noises.

**(Choice A)** Acetylcholine release is inhibited by the botulinum toxin from *C botulinum*, leading to the flaccid paralysis seen in clinical botulism.

**(Choices B and C)** Neither dopamine nor glutamate release has been linked to toxin effects in humans.

**(Choice E)** Serotonin release from enterochromaffin cells in the gastrointestinal tract is stimulated by *Vibrio cholera* enterotoxin. This increased serotonin release contributes to the extreme fluid secretion seen in cholera.


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**(Choice E)** Serotonin release from enterochromaffin cells in the gastrointestinal tract is stimulated by *Vibrio cholera* enterotoxin. This increased serotonin release contributes to the extreme fluid secretion seen in cholera.

**Educational objective:**
Tetanospasmin is a neuro-exotoxin released by *Clostridium tetani*. The toxin blocks the release of glycine and gamma-aminobutyric acid (GABA) from the spinal inhibitory interneurons that regulate the lower motor neurons. These disinhibited motor neurons cause increased activation of muscles, leading to spasms and hyperreflexia.

| Pathophysiology | Nervous System | Tetanus |
|---|---|---|
| Subject | System | Topic |


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A 34-year-old man comes to the emergency department due to 2 weeks of slowly progressive global headache, malaise, and fevers. He has also had unintentional weight loss over the past several months. The patient has a history of injection drug use and was diagnosed with HIV 3 years ago. He has not been compliant with antiretroviral therapy. Temperature is 38.3 C (100.9 F). Examination shows white patches on the oropharyngeal mucosa and mild generalized lymphadenopathy. Brain imaging reveals no intracranial masses. India ink staining of cerebrospinal fluid demonstrates spherical yeast forms with thick capsules. Which of the following is the most likely site of primary infection in this patient?

A. Intestine
B. Lungs
C. Nasopharynx
D. Oral cavity
E. Skin

Submit



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A. Intestine (2%)
B. Lungs (61%)
C. Nasopharynx (27%)
D. Oral cavity (6%)
E. Skin (2%)

61%
01 min, 21 secs
01/12/2021


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| Characteristics of pathogenic yeasts | | |
|---|---|---|
| **Organism** | **Morphology** | **Clinical syndromes** |
| ***Candida*** | Pseudohyphae with blastoconidia | Mucocutaneous or invasive infections (eg, candidemia due to vascular catheter) |
| ***Blastomyces*** | Yeast with broad-based budding | Inhaled → skin & bone |
| ***Coccidioides*** | Spherules with endospores | Transient pulmonary syndrome → meninges & bone |
| ***Cryptococcus*** | Encapsulated yeast | Meningitis in immunocompromised (eg, advanced AIDS) |
| ***Histoplasma*** | Small, oval yeast within macrophages | Mostly subclinical but can cause community-acquired pneumonia → dissemination |

***Cryptococcus neoformans*** is a low-virulence yeast with a thick polysaccharide capsule. The organism resides in soil contaminated by bird (eg, pigeon) droppings, and human exposure primarily occurs due to


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***Cryptococcus neoformans*** is a low-virulence yeast with a thick polysaccharide capsule. The organism resides in soil contaminated by bird (eg, pigeon) droppings, and human exposure primarily occurs due to **inhalation** into the **lungs**. Alveolar macrophages ingest the yeast, travel to draining lymph nodes, and activate CD4 T-lymphocytes that subsequently promote granuloma formation and enhanced destruction of the pathogen within phagolysosomes. Although a minority of patients clear the organism, most individuals develop **life-long latent infection**, similar to tuberculosis; those who are severely immunocompromised (eg, **AIDS** with CD4 count <100/mm$^3$) are at high risk for reactivation.

**Cryptococcal meningitis** primarily occurs when *C neoformans* reactivates from a latent pulmonary focus, spreads through the circulation, and penetrates the endothelial cells of the cerebral capillaries. Replication within the CNS leads to slowly worsening headache, fever, and confusion. Visualization of the organism (ie, round/oval yeast with a thick capsule) on cerebrospinal fluid samples using India ink stain confirms the diagnosis. Polysaccharide antigen (cryptococcal antigen) testing can also be helpful.

**(Choice A)** Ingestion of *C neoformans* in contaminated food can lead to infection. However, this route is much less common than inhalation into the lungs.

**(Choice C)** Acute bacterial meningitis is caused primarily by pathogens (eg, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*) that colonize the nasopharynx. Manifestations of acute


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diagnosis. Polysaccharide antigen (cryptococcal antigen) testing can also be helpful.

**(Choice A)** Ingestion of *C neoformans* in contaminated food can lead to infection. However, this route is much less common than inhalation into the lungs.

**(Choice C)** Acute bacterial meningitis is caused primarily by pathogens (eg, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*) that colonize the nasopharynx. Manifestations of acute bacterial meningitis usually include the rapid onset fever, neck stiffness, and altered mental state. Cerebrospinal fluid Gram stain will be positive.

**(Choice D)** Patients who have untreated AIDS often develop multiple opportunistic infections; the white patches on this patient's oral mucosa likely indicate oropharyngeal candidiasis. Superficial *Candida* infections rarely cause invasive disease. In addition, *Candida* does not have a thick polysaccharide capsule and is not seen on India ink stain.

**(Choice E)** Skin bacteria (eg, *Staphylococcus aureus*, *Streptococcus pyogenes*) can cause systemic infection following skin breakdown. Systemic infection from skin fungus (eg, *Candida*) following skin breakdown is uncommon. This patient's encapsulated yeast on India Ink stain indicates *Cryptococcus*, making inhalation the most likely route of infection.

**Educational objective:**



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**(Choice E)** Skin bacteria (eg, *Staphylococcus aureus*, *Streptococcus pyogenes*) can cause systemic infection following skin breakdown. Systemic infection from skin fungus (eg, *Candida*) following skin breakdown is uncommon. This patient's encapsulated yeast on India Ink stain indicates *Cryptococcus*, making inhalation the most likely route of infection.

**Educational objective:**

*Cryptococcus neoformans* is a yeast with a thick polysaccharide capsule that is found primarily in soil contaminated by bird droppings. Inhalation of the pathogen into the lungs leads to asymptomatic primary infection usually followed by life-long latent infection. However, immunocompromised (eg, advanced AIDS) patients are at high risk for reactivation with spread to the CNS.

**References**

- Molecular mechanisms of cryptococcal meningitis.

Microbiology  Nervous System  Meningitis



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A 65-year-old man is evaluated for right lower extremity weakness and difficulty walking. The patient has a history of hypertension, type 2 diabetes mellitus, and osteoarthritis. He has smoked a pack of cigarettes daily for 30 years. During physical examination, the lateral border of his right sole is stroked using the blunt tip of a reflex hammer. The maneuver, starting near the heel and proceeding to the base of the fifth toe, elicits extension of the great toe and fanning out of the other toes. Which of the following additional findings is most likely to be observed in this patient's right lower extremity?

A. Decreased muscle girth compared to the left side
B. Increased briskness of deep tendon reflexes
C. Increased muscle rigidity with rhythmic interruptions
D. Pronounced weakness of extensor muscles compared to flexors
E. Spontaneous, intermittent contractions of muscle fibers

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A 65-year-old man is evaluated for right lower extremity weakness and difficulty walking. The patient has a history of hypertension, type 2 diabetes mellitus, and osteoarthritis. He has smoked a pack of cigarettes daily for 30 years. During physical examination, the lateral border of his right sole is stroked using the blunt tip of a reflex hammer. The maneuver, starting near the heel and proceeding to the base of the fifth toe, elicits extension of the great toe and fanning out of the other toes. Which of the following additional findings is most likely to be observed in this patient's right lower extremity?

A. ~~Decreased muscle girth compared to the left side~~ (3%)

✓ B. Increased briskness of deep tendon reflexes (83%)

C. ~~Increased muscle rigidity with rhythmic interruptions~~ (5%)

D. ~~Pronounced weakness of extensor muscles compared to flexors~~ (2%)

E. ~~Spontaneous, intermittent contractions of muscle fibers~~ (5%)

Correct

83% Answered correctly

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01/10/2021 Last Updated



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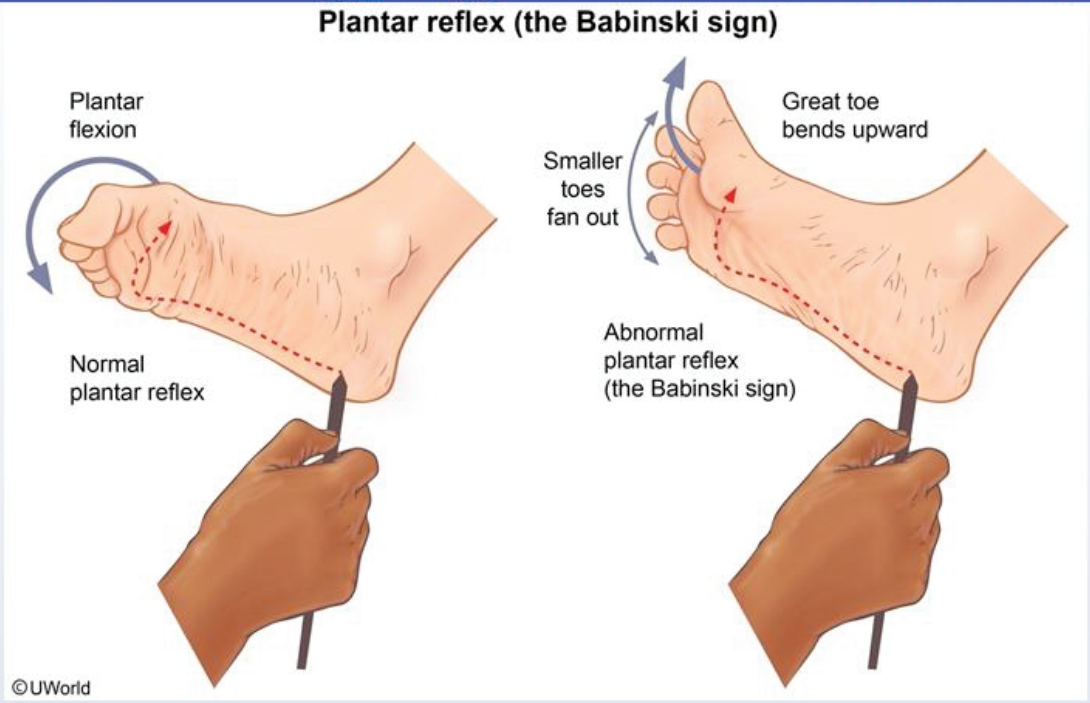


The **plantar reflex** (Babinski sign) is assessed by firmly stroking the plantar surface of the lateral foot from the heel to the ball. Plantar flexion of the toes is normal; **dorsiflexion** with or without fanning of the toes is considered abnormal and indicates an **upper motor neuron lesion**. Children age <12 months also exhibit


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The **plantar reflex** (Babinski sign) is assessed by firmly stroking the plantar surface of the lateral foot from the heel to the ball. Plantar flexion of the toes is normal; **dorsiflexion** with or without fanning of the toes is considered abnormal and indicates an **upper motor neuron lesion**. Children age <12 months also exhibit a positive response, which is considered normal and reflects incomplete myelination of the corticospinal tract.

Upper motor neurons (UMNs) originate in the cerebral cortex and are responsible for the initiation of voluntary movement. UMN fibers travel through the brainstem and spinal cord to reach lower motor neurons (eg, cranial nerves, spinal nerves), which then innervate muscle fibers. UMN injury can occur anywhere proximal to the anterior horn; common etiologies include stroke (which likely occurred in this patient with multiple risk factors), multiple sclerosis, or spinal cord transection.

Other signs of UMN injury include **hyperreflexia**, spastic paralysis, **increased muscle tone**, clasp-knife rigidity (increased muscle tension with sudden release on passive flexion), and **pyramidal weakness** (weakness is more pronounced in **lower extremity flexors** and **upper extremity extensors**). Upper extremity supination is also typically weaker than pronation, resulting in pronator drift.

**(Choices A and E)** Lower motor nerve lesions are most commonly due to trauma involving the peripheral nerves. Manifestations include muscle weakness/paralysis with hypotonia, suppressed or absent deep


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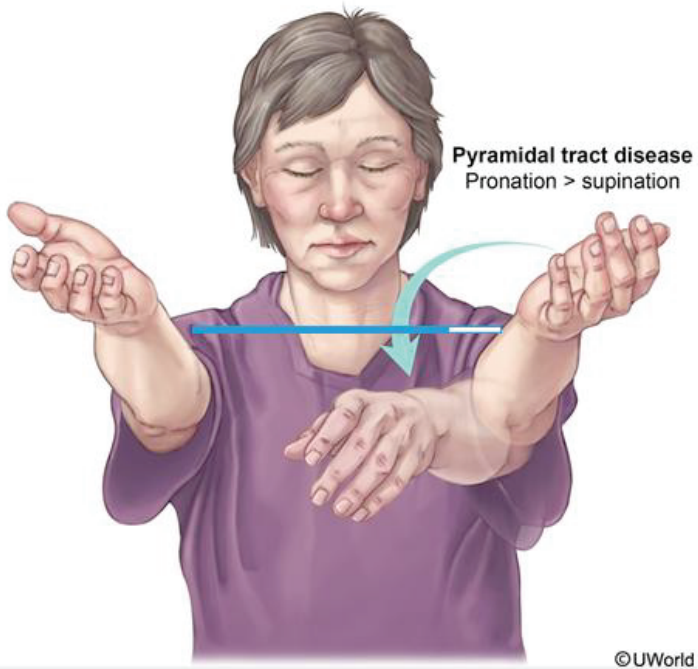
Pronator drift

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**(Choices A and E)** Lower motor nerve lesions are most commonly due to trauma involving the peripheral nerves. Manifestations include muscle weakness/paralysis with hypotonia, suppressed or absent deep tendon reflexes, and muscle atrophy. Fasciculations (brief, spontaneous contractions of small groups of muscle fibers) also occur due to denervation of the affected muscles. However, the plantar reflex in lower motor lesions will be downgoing or indifferent (ie, no response).

**(Choice C)** Cogwheel rigidity (increased muscle rigidity with rhythmic interruptions noted on passive limb movement) is seen with lesions in the extrapyramidal tracts, which modulate motor neuron activity. This sign is classically seen in Parkinson disease.

**(Choice D)** In upper motor neuron lesions, lower extremity weakness is typically more pronounced in the flexors than the extensors.

**Educational objective:**
Upper motor neuron signs include abnormal plantar flexion (Babinski sign), spastic paralysis, increased muscle tone, clasp-knife rigidity, hyperreflexia, pronator drift, and pyramidal weakness (weakness more pronounced in lower extremity flexors and upper extremity extensors). Lower motor neuron signs include flaccid paralysis, weakness with hypotonia and muscle atrophy, fasciculations, and suppressed or absent reflexes.


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A 22-year-old man is undergoing surgical repair of an inguinal hernia. Anesthesia is induced and an endotracheal tube is placed. He then develops severe spasm of the masseter muscles, and there is a dramatic increase in expired carbon dioxide measured from the endotracheal tube. His core body temperature begins to increase and is now 38.9 C (102 F). Which of the following is the most likely underlying mechanism leading to elevated body temperature in this patient?

A. Acute elevation of circulating free T4
B. Change in hypothalamic set point
C. Excessive myoplasmic calcium accumulation
D. Impaired cutaneous vasodilation
E. Increased serotonergic activity in the CNS

Submit


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A 22-year-old man is undergoing surgical repair of an inguinal hernia. Anesthesia is induced and an endotracheal tube is placed. He then develops severe spasm of the masseter muscles, and there is a dramatic increase in expired carbon dioxide measured from the endotracheal tube. His core body temperature begins to increase and is now 38.9 C (102 F). Which of the following is the most likely underlying mechanism leading to elevated body temperature in this patient?

A. Acute elevation of circulating free T4 (1%)
B. Change in hypothalamic set point (11%)
✓ C. Excessive myoplasmic calcium accumulation (77%)
D. Impaired cutaneous vasodilation (4%)
E. Increased serotonergic activity in the CNS (5%)

Correct

77%
Answered correctly

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Time Spent

09/22/2020
Last Updated



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| Malignant hyperthermia | |
|---|---|
| **Pathophysiology** | • Genetic mutation of ryanodine receptors<br>• Triggered by inhalational anesthetics & succinylcholine<br>• Unregulated sarcoplasmic calcium release → sustained muscle contraction |
| **Clinical manifestations** | • Masseter muscle spasm<br>• Widespread muscle contraction (rigidity)<br>• Hypercarbia<br>• Rhabdomyolysis → hyperkalemia & acute renal failure<br>• Hyperthermia (late manifestation) |
| **Treatment** | • Immediate cessation of causative anesthetic<br>• Dantrolene |

This patient with masseter muscle spasm, acute hypercarbia, and elevated temperature shortly after induction of anesthesia likely has **malignant hyperthermia** (MH), a condition characterized by excessive


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This patient with masseter muscle spasm, acute hypercarbia, and elevated temperature shortly after induction of anesthesia likely has **malignant hyperthermia** (MH), a condition characterized by excessive muscle contracture.

Normally, muscle contraction is mediated by a cascade of events:

- Membrane depolarization **releases calcium** from the sarcoplasmic reticulum into the intracellular space
- Calcium binds to troponin to expose myosin bridging sites
- Exposed myosin cross-links to actin and contracts
- Sarcoplasmic reticulum calcium ATPase reuptakes calcium to reverse this binding and cause relaxation

In patients with MH, exposure to certain **anesthetic agents** (eg, succinylcholine, inhalational gasses) causes unregulated passage of calcium from the sarcoplasmic reticulum into the intracellular space. **Excessive myoplasmic calcium accumulation** results in sustained muscle contraction, which is often first noted in the masseter.

**Sustained muscle contraction** leads to increased cellular metabolism, which causes **hypercarbia** and


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causes unregulated passage of calcium from the sarcoplasmic reticulum into the intracellular space. **Excessive myoplasmic calcium accumulation** results in sustained muscle contraction, which is often first noted in the masseter.

**Sustained muscle contraction** leads to increased cellular metabolism, which causes **hypercarbia** and acidosis. Muscle hypermetabolism consumes ATP and leads to **excessive heat production**. Once ATP and oxygen stores are depleted, muscle breakdown (ie, rhabdomyolysis) occurs, which releases potassium, myoglobin, and creatine kinase, leading to a further cascade (eg, arrhythmias, acute renal failure, disseminated intravascular coagulation) that may be fatal. **Dantrolene** is used to treat MH because it blocks further release of calcium into the intracellular space.

**(Choice A)** Thyroid storm (ie, thyrotoxic crisis) can be precipitated by surgery. Hyperpyrexia occurs because excessive circulating levels of T3 and T4 increase cellular metabolism and adrenergic tone. However, thyroid storm does not cause sustained muscle contractions.

**(Choice B)** A true fever results from a change in the hypothalamic set point, typically due to an infection (not anesthesia). Shivering may occur, but not sustained muscle contraction or acute hypercarbia.

**(Choice D)** Heat dissipation occurs primarily by cutaneous vasodilation and sweating. These mechanisms can be impaired by aging or medications (eg, atropine). During an MH crisis, cutaneous heat removal is


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**(Choice B)** A true fever results from a change in the hypothalamic set point, typically due to an infection (not anesthesia). Shivering may occur, but not sustained muscle contraction or acute hypercarbia.

**(Choice D)** Heat dissipation occurs primarily by cutaneous vasodilation and sweating. These mechanisms can be impaired by aging or medications (eg, atropine). During an MH crisis, cutaneous heat removal is unaffected, but heat production far outstrips heat dissipation.

**(Choice E)** Excessive serotonergic activity in the CNS can result in hyperpyrexia (due to serotonin syndrome). However, it classically presents with hyperreflexia and clonus (rather than rigidity) and is seen in patients taking serotonergic medications (eg, selective serotonin reuptake inhibitors, tricyclic antidepressants), especially in combination, rather than with anesthesia.

**Educational objective:**
In patients with malignant hyperthermia, exposure to certain anesthetic agents (eg, succinylcholine, inhalational gasses) causes unregulated passage of calcium from the sarcoplasmic reticulum into the intracellular space. This results in sustained muscle contraction that leads to hypercarbia, hyperthermia, and acidosis.

**References**



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A 58-year-old man comes to the office due to lower extremity pain. The patient began experiencing tingly discomfort in his toes a year ago, especially at night when the sheets touched his skin. Since then, the symptoms have progressed to a burning and stabbing pain in his feet and lower legs. He was diagnosed with diabetes mellitus 8 years ago and hypertension 3 years ago. The patient quit smoking 20 years ago and does not use alcohol. Blood pressure is 126/70 mm Hg and pulse is 68/min. Lower extremity examination shows normal-appearing skin. Touching the feet elicits a sensation of burning pain. There is loss of vibration sensation in the toes, and the ankle reflex is absent bilaterally. Which of the following is the best initial pharmacotherapy for this patient's symptoms?

A. Amitriptyline
B. Clonazepam
C. Fluoxetine
D. Naproxen
E. Oxycodone
F. Pyridoxine


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symptoms have progressed to a burning and stabbing pain in his feet and lower legs. He was diagnosed with diabetes mellitus 8 years ago and hypertension 3 years ago. The patient quit smoking 20 years ago and does not use alcohol. Blood pressure is 126/70 mm Hg and pulse is 68/min. Lower extremity examination shows normal-appearing skin. Touching the feet elicits a sensation of burning pain. There is loss of vibration sensation in the toes, and the ankle reflex is absent bilaterally. Which of the following is the best initial pharmacotherapy for this patient's symptoms?

- A. Amitriptyline (62%)
- B. Clonazepam (3%)
- C. Fluoxetine (9%)
- D. Naproxen (6%)
- E. Oxycodone (2%)
- F. Pyridoxine (14%)

Correct

62%

58 secs

01/27/2021



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| Distal symmetric polyneuropathy | |
|---|---|
| **Triggers** | • Diabetes mellitus (diabetic neuropathy)<br>• Long-standing HIV infection<br>• Uremia<br>• Medications (eg, fluoroquinolones, metronidazole)<br>• Chemotherapy (eg, cisplatin, paclitaxel)<br>• Toxicity (eg, alcohol abuse, heavy metal exposure) |
| **Pathophysiology** | • Damage to distal sensory peripheral nerve axons |
| **Manifestations** | • Symptoms begin in toes/feet; progresses proximally over time<br>• Distal numbness, tingling, pins & needles sensation<br>• ↓ Pain, temperature, touch & vibration sensation<br>• ↓ Ankle/Babinski reflexes |
| **Treatment** | • Treat underlying cause<br>• Pain management: gabapentinoid, tricyclic antidepressant, duloxetine &/or capsaicin cream |



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| | |
|---|---|
| | capsaicin cream |

This patient with long-standing diabetes mellitus has tingling/burning pain in the feet, loss of vibration sensation, and loss of ankle reflexes, indicating **distal symmetric polyneuropathy** (diabetic neuropathy). Long-standing diabetes mellitus is often associated with damage to the **distal axons of sensory neurons** due to the accumulation of cross-linked glycosylated serum proteins in the vaso nervorum, which causes inflammation, vasoconstriction, and neuronal oxidative stress. Initial symptoms include tingling, numbness, and **burning pain** in the toes and/or feet. Sensation to pain, light touch, temperature, vibration, and proprioception are generally diminished in the affected area. Babinski and ankle reflex are often absent.

Treatment includes **glycemic control** and **foot care** to limit the development of ulcers and need for amputation. Patients with **painful** neuropathy also typically receive a serotonin-norepinephrine reuptake inhibitor (eg, duloxetine, venlafaxine), a gabapentinoid (eg, pregabalin, gabapentin), or a tricyclic antidepressant such as **amitriptyline**. Amitriptyline modulates pain transmission by inhibiting voltage-gated sodium channels in sensory nerves, blocking NMDA (excitatory) receptors in the spinal cord, and altering norepinephrine signaling in the brain.

**(Choice B)** Benzodiazepines (eg, clonazepam) are often used for anxiety, muscle relaxation, or nausea. They are not typically used for neuropathic pain.


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They are not typically used for neuropathic pain.

**(Choice C)** Although selective serotonin reuptake inhibitors (eg, fluoxetine) are often used for depression and anxiety, they are not often employed for neuropathic pain. In contrast, serotonin-norepinephrine reuptake inhibitors (eg, duloxetine, venlafaxine) are often used as first-line treatment to manage painful diabetic neuropathy; these agents alter central transmission of pain by increasing norepinephrine in the central synapses.

**(Choice D)** Nonsteroidal anti-inflammatory drugs such as naproxen are prescribed for acute painful conditions such as back pain, muscle strain, or bone fracture. However, they have limited efficacy for neuropathic pain.

**(Choice E)** Opioid pain medications (eg, oxycodone) are not recommended for most patients with neuropathic pain due to their questionable efficacy and risk of dependence/abuse/addiction. Patients with neuropathic pain should first be given a trial of an antidepressant or gabapentinoid.

**(Choice F)** Certain patients taking isoniazid require pyridoxine supplementation to prevent the development of drug-induced peripheral neuropathy. This patient is not taking isoniazid; therefore, pyridoxine supplementation would not be helpful.

**Educational objective:**


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neuropathic pain.

**(Choice E)** Opioid pain medications (eg, oxycodone) are not recommended for most patients with neuropathic pain due to their questionable efficacy and risk of dependence/abuse/addiction. Patients with neuropathic pain should first be given a trial of an antidepressant or gabapentinoid.

**(Choice F)** Certain patients taking isoniazid require pyridoxine supplementation to prevent the development of drug-induced peripheral neuropathy. This patient is not taking isoniazid; therefore, pyridoxine supplementation would not be helpful.

**Educational objective:**
Patients with long-standing, poorly controlled diabetes mellitus are at high risk for developing distal symmetric polyneuropathy (diabetic neuropathy). Symptoms generally include progressive numbness, tingling, and burning/stabbing pain in the feet and/or toes that progresses proximally. Painful neuropathy is treated with serotonin-norepinephrine reuptake inhibitors, gabapentinoids, or tricyclic antidepressants.

| Pharmacology | Nervous System | Peripheral neuropathy |
|---|---|---|
| Subject | System | Topic |

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A 1-month-old, full-term boy is brought to the emergency department by his mother due to difficulty awakening him. The mother says that the infant was left alone for a few minutes this morning and rolled off a bed. Since then, he has been sleepy and less active than usual. Physical examination shows a lethargic boy with a large, full anterior fontanelle. Bilateral retinal hemorrhages are seen on funduscopic examination. Which of the following should be strongly suspected in this patient?

A. Abusive head trauma
B. Bacterial meningitis
C. Idiopathic thrombocytopenic purpura
D. Neonatal vitamin K deficiency
E. Retinoblastoma
F. Unintentional head injury

Submit



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A 1-month-old, full-term boy is brought to the emergency department by his mother due to difficulty awakening him. The mother says that the infant was left alone for a few minutes this morning and rolled off a bed. Since then, he has been sleepy and less active than usual. Physical examination shows a lethargic boy with a large, full anterior fontanelle. Bilateral retinal hemorrhages are seen on funduscopic examination. Which of the following should be strongly suspected in this patient?

- A. Abusive head trauma (69%)
- B. Bacterial meningitis (1%)
- C. Idiopathic thrombocytopenic purpura (0%)
- D. Neonatal vitamin K deficiency (11%)
- E. Retinoblastoma (2%)
- F. Unintentional head injury (14%)

Correct

69%
Answered correctly

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Time Spent

12/14/2020
Last Updated



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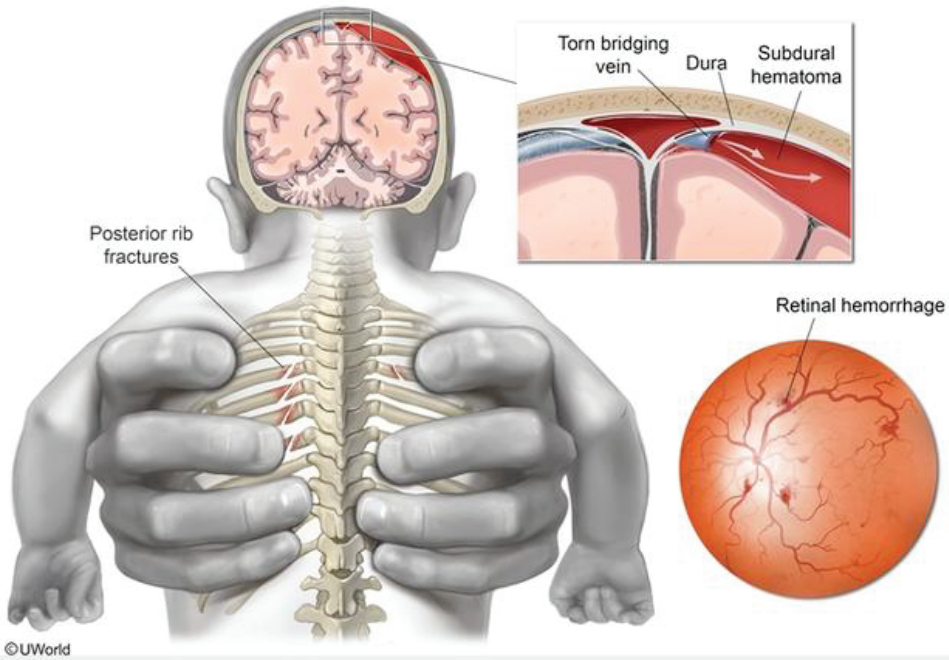
Exhibit Display

Shaking mechanism in abusive trauma

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**Abusive head trauma (AHT)**, formerly known as "shaken baby syndrome," is inflicted intracranial injury due to blunt force trauma or **vigorous shaking** in a to-and-fro fashion. The resultant injuries are due to infants' unique anatomic features. Infants have larger heads, enlarged subarachnoid spaces, higher brain water content, and decreased cervical muscle tone compared to older children. These factors lead to increased movement of the immature brain in relation to the skull, resulting in **tearing of the bridging veins** and subdural hemorrhages. Because AHT may occur repeatedly over weeks to months, acute on chronic subdural hemorrhages are often seen.

The shaking motion also results in **retinal hemorrhages** due to rupture of congested retinal veins. Retinal hemorrhages are highly suggestive of AHT. Infants' ribs are flexible and pliable, and **posterior rib fractures** are also alarming for trauma by a perpetrator's grasp on the torso. In addition, the history provided by this patient's parent does not match his developmental age, as rolling over is not typical before age 4 months. Furthermore, an accidental fall **(Choice F)** from a bed would generally not be sufficient to cause a large intracranial hemorrhage resulting in altered mental status and would not explain retinal hemorrhages.

**(Choice B)** Although bacterial meningitis can cause lethargy, patients are typically febrile.

**(Choice C)** Idiopathic thrombocytopenic purpura, caused by platelet autoantibody formation, presents with


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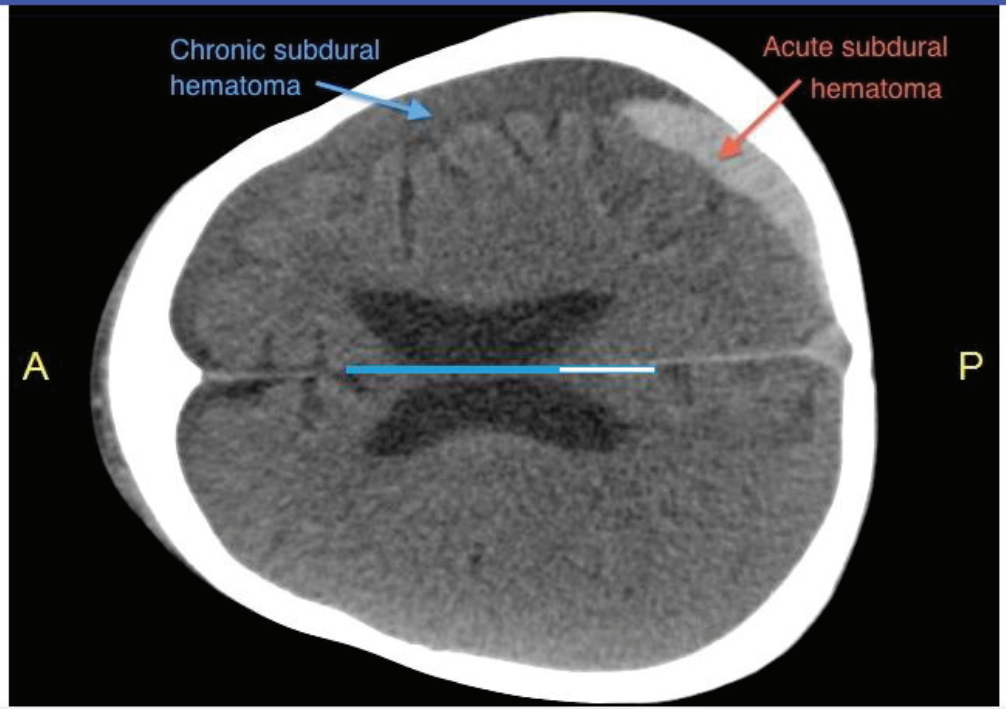


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(Choice C) Idiopathic thrombocytopenic purpura, caused by platelet autoantibody formation, presents with



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**(Choice B)** Although bacterial meningitis can cause lethargy, patients are typically febrile.

**(Choice C)** Idiopathic thrombocytopenic purpura, caused by platelet autoantibody formation, presents with petechiae, ecchymoses, and bleeding after minor trauma. Intracranial hemorrhage is rare and retinal hemorrhages are not seen.

**(Choice D)** All newborns are vitamin K-deficient and are given prophylactic vitamin K injections at birth. Although vitamin K deficiency can present with intracranial, umbilical, and gastrointestinal bleeding, retinal hemorrhages are not seen.

**(Choice E)** Retinoblastoma is the most common ocular tumor of infancy and presents with absence of the "red reflex" on physical examination. Lethargy and retinal hemorrhage are not seen.

**Educational objective:**
Abusive head trauma can be caused by vigorous shaking of an infant and results in **subdural hemorrhage** (due to tearing of bridging veins) and **retinal hemorrhages**. Additional red flags are injuries inconsistent with history or developmental age.

**References**

- Abusive head trauma in children: a literature review.



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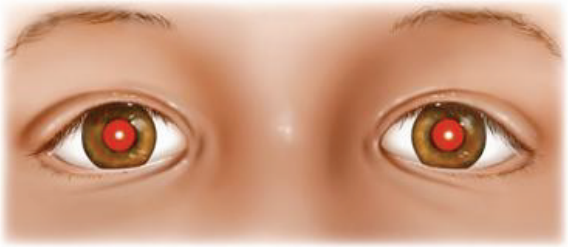
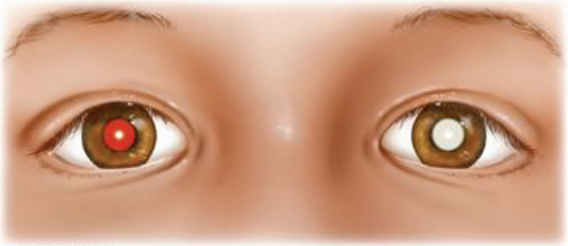
## Exhibit Display

**Normal eyes & white reflex**



**Normal eyes**
Red reflexes & corneal light reflexes are equal.



**Absent reflex**
White reflex on abnormal eye can result from opacities of the lens (eg, cataract) or tumor (eg, retinoblastoma).

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A 43-year-old man with a history of HIV infection who is noncompliant with highly active antiretroviral therapy comes to the office due to progressive memory loss and cognitive decline over the last several years. The patient has problems with attention, concentration, and speech. In the past few months, he has become more apathetic and increasingly lethargic. More recently, he has had difficulty with balance and has fallen on multiple occasions. The patient has had no headache, tremor, change in vision, fever, nausea/vomiting, or urinary incontinence. His brother has a history of severe intellectual disability and epilepsy. Mini-Mental State Examination score is 18/30, and the patient appears emotionally blunted. He also has postural instability and difficulty performing fine motor tasks. Noncontrast head CT scan reveals diffuse cortical atrophy with some enlargement of the ventricles, as shown in the exhibits. This patient's condition can be best described as which of the following?

A. Communicating hydrocephalus
B. Hydrocephalus ex-vacuo
C. Lissencephaly
D. Noncommunicating hydrocephalus
E. Pseudotumor cerebri


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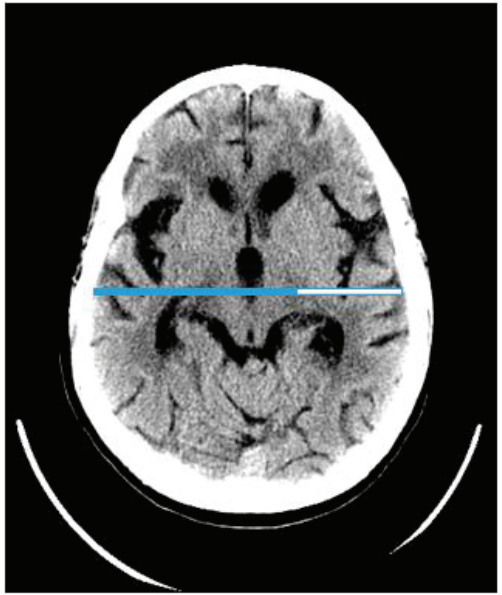
Exhibit Display

Exhibit 1 Exhibit 2



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E. Pseudotumor cerebri



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become more apathetic and increasingly lethargic. More recently, he has had difficulty with balance and has fallen on multiple occasions. The patient has had no headache, tremor, change in vision, fever, nausea/vomiting, or urinary incontinence. His brother has a history of severe intellectual disability and epilepsy. Mini-Mental State Examination score is 18/30, and the patient appears emotionally blunted. He also has postural instability and difficulty performing fine motor tasks. Noncontrast head CT scan reveals diffuse cortical atrophy with some enlargement of the ventricles, as shown in the exhibits. This patient's condition can be best described as which of the following?

A. Communicating hydrocephalus
B. Hydrocephalus ex-vacuo
C. Lissencephaly
D. Noncommunicating hydrocephalus
E. Pseudotumor cerebri
F. Transtentorial (uncal) herniation

Submit



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become more apathetic and increasingly lethargic. More recently, he has had difficulty with balance and has fallen on multiple occasions. The patient has had no headache, tremor, change in vision, fever, nausea/vomiting, or urinary incontinence. His brother has a history of severe intellectual disability and epilepsy. Mini-Mental State Examination score is 18/30, and the patient appears emotionally blunted. He also has postural instability and difficulty performing fine motor tasks. Noncontrast head CT scan reveals diffuse cortical atrophy with some enlargement of the ventricles, as shown in the exhibits. This patient's condition can be best described as which of the following?

- A. Communicating hydrocephalus
- B. Hydrocephalus ex-vacuo
- C. Lissencephaly
- D. Noncommunicating hydrocephalus
- E. Pseudotumor cerebri
- F. Transtentorial (uncal) herniation

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become more apathetic and increasingly lethargic. More recently, he has had difficulty with balance and has fallen on multiple occasions. The patient has had no headache, tremor, change in vision, fever, nausea/vomiting, or urinary incontinence. His brother has a history of severe intellectual disability and epilepsy. Mini-Mental State Examination score is 18/30, and the patient appears emotionally blunted. He also has postural instability and difficulty performing fine motor tasks. Noncontrast head CT scan reveals diffuse cortical atrophy with some enlargement of the ventricles, as shown in the exhibits. This patient's condition can be best described as which of the following?

- A. Communicating hydrocephalus (10%)
- ✓ B. Hydrocephalus ex-vacuo (75%)
- C. Lissencephaly (3%)
- D. Noncommunicating hydrocephalus (6%)
- E. Pseudotumor cerebri (3%)
- F. Transtentorial (uncal) herniation (1%)



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Cerebrospinal fluid (CSF) circulates in the ventricular system and subarachnoid space and is constantly secreted by the choroid plexus and absorbed by granulations of the arachnoid mater. Hydrocephalus is defined as enlargement of the ventricles (with or without elevated pressure) caused by either central neuronal volume loss (eg, **hydrocephalus ex-vacuo**) or excessive CSF accumulation. Patients with neurodegenerative diseases (eg, **AIDS dementia**) can develop hydrocephalus ex-vacuo due to significant **cortical atrophy**, which allows the ventricles to expand while maintaining **normal CSF pressure**.

Ventricular enlargement caused by excessive CSF accumulation typically occurs due to obstructed CSF circulation (noncommunicating hydrocephalus) or absorption (communicating hydrocephalus). In communicating hydrocephalus, CSF flows freely between the ventricles and subarachnoid space, but there is decreased CSF reabsorption at the arachnoid granulations **(Choice A)**. There are 2 major types of communicating hydrocephalus:

- Normal-pressure hydrocephalus (NPH) is caused by a chronic reduction in CSF absorption at the arachnoid villi, resulting in enlargement of the ventricles out of proportion to the overlying cortical atrophy. Because the impaired CSF absorption is chronic, the ventricles enlarge slowly, allowing the CSF pressure to normalize. Patients with NPH typically present with early ataxia followed by frontal


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atrophy. Because the impaired CSF absorption is chronic, the ventricles enlarge slowly, allowing the CSF pressure to normalize. Patients with NPH typically present with early ataxia followed by frontal lobe dementia and urinary incontinence.

- High-pressure hydrocephalus results from more acute impairment in CSF absorption (eg, cerebral venous sinus thrombosis, meningitis, acute subarachnoid hemorrhage) and typically presents with a change in mental status, seizure, headache, and focal neurologic deficits.

**(Choice C)** Lissencephaly (agyria) is a congenital absence of gyri. This condition is typically accompanied by severe mental retardation and seizures. On gross examination and imaging, the brain surface has a smooth appearance.

**(Choice D)** Obstruction of CSF flow within or between the ventricles and subarachnoid space is termed noncommunicating hydrocephalus. Congenital abnormalities (eg, aqueductal stenosis, Arnold-Chiari malformation) and tumors can lead to this type of hydrocephalus, resulting in symptoms of elevated intracranial pressure. In noncommunicating hydrocephalus, only the ventricles that are proximal to the obstruction are dilated.

**(Choice E)** Pseudotumor cerebri (idiopathic intracranial hypertension) refers to elevated intracranial pressure in the absence of ventricular enlargement on imaging. This disorder classically presents in


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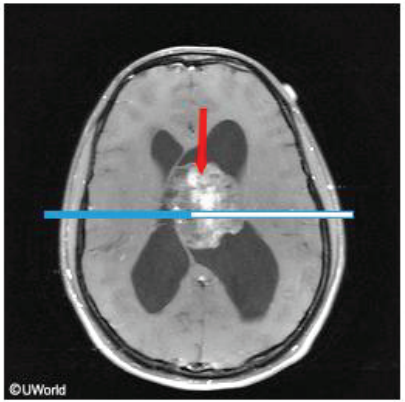


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pressure in the absence of ventricular enlargement on imaging. This disorder classically presents in



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obstruction are dilated.

**(Choice E)** Pseudotumor cerebri (idiopathic intracranial hypertension) refers to elevated intracranial pressure in the absence of ventricular enlargement on imaging. This disorder classically presents in young, obese women with headache, papilledema, and possible visual loss due to optic neuropathy.

**(Choice F)** Transtentorial (uncal) herniation can occur due to an intracranial mass (eg, tumor, hemorrhage) or cerebral edema. This may lead to compression of the ipsilateral oculomotor nerve and posterior cerebral artery. A fixed, dilated pupil on the same side as the lesion is often the first sign of uncal herniation.

**Educational objective:**

Hydrocephalus is an enlargement of the ventricles (with or without elevated pressure) caused by either neuronal volume loss (eg, hydrocephalus ex-vacuo) or excessive cerebrospinal fluid accumulation (due to flow obstruction or impaired absorption). Neurodegenerative diseases (eg, AIDS dementia) can be associated with hydrocephalus ex-vacuo due to significant cortical atrophy, which allows the ventricles to expand while maintaining normal pressure.

| Pathology | Nervous System | Hydrocephalus |
|---|---|---|
| Subject | System | Topic |



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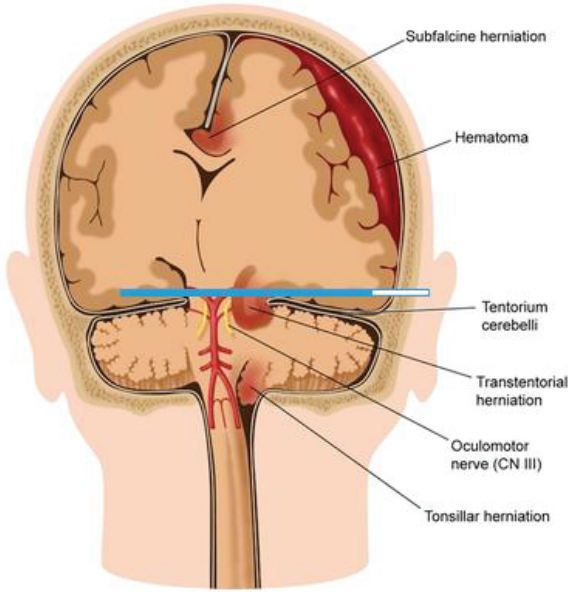
obstruction are dilated.

Exhibit Display

Major herniations of the brain

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Subject System Topic



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A 7-year-old boy is brought to the emergency department after injuring his right knee in a bicycle accident. Physical examination shows a swollen right knee with abrasion of the overlying skin. Distal motor and sensory innervation are intact, and popliteal and pedal pulses are normal. No other significant trauma is noted. X-ray reveals a nondisplaced patellar fracture. The patient is referred to orthopedics and placed in a leg cylinder cast. On follow-up a week after cast placement, he has paresthesia and numbness of the dorsum of the right foot along with weakness in foot dorsiflexion and eversion. Which of the following is the most likely site of nerve compression in this patient?

A. Anterior compartment of the leg
B. Fibular neck
C. Lateral compartment of the leg
D. Medial malleolus
E. Popliteal fossa

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A 7-year-old boy is brought to the emergency department after injuring his right knee in a bicycle accident. Physical examination shows a swollen right knee with abrasion of the overlying skin. Distal motor and sensory innervation are intact, and popliteal and pedal pulses are normal. No other significant trauma is noted. X-ray reveals a nondisplaced patellar fracture. The patient is referred to orthopedics and placed in a leg cylinder cast. On follow-up a week after cast placement, he has paresthesia and numbness of the dorsum of the right foot along with weakness in foot dorsiflexion and eversion. Which of the following is the most likely site of nerve compression in this patient?

- A. Anterior compartment of the leg (14%)
- ✓ B. Fibular neck (60%)
- C. Lateral compartment of the leg (18%)
- D. Medial malleolus (2%)
- E. Popliteal fossa (4%)

60% 51 secs 02/14/2021


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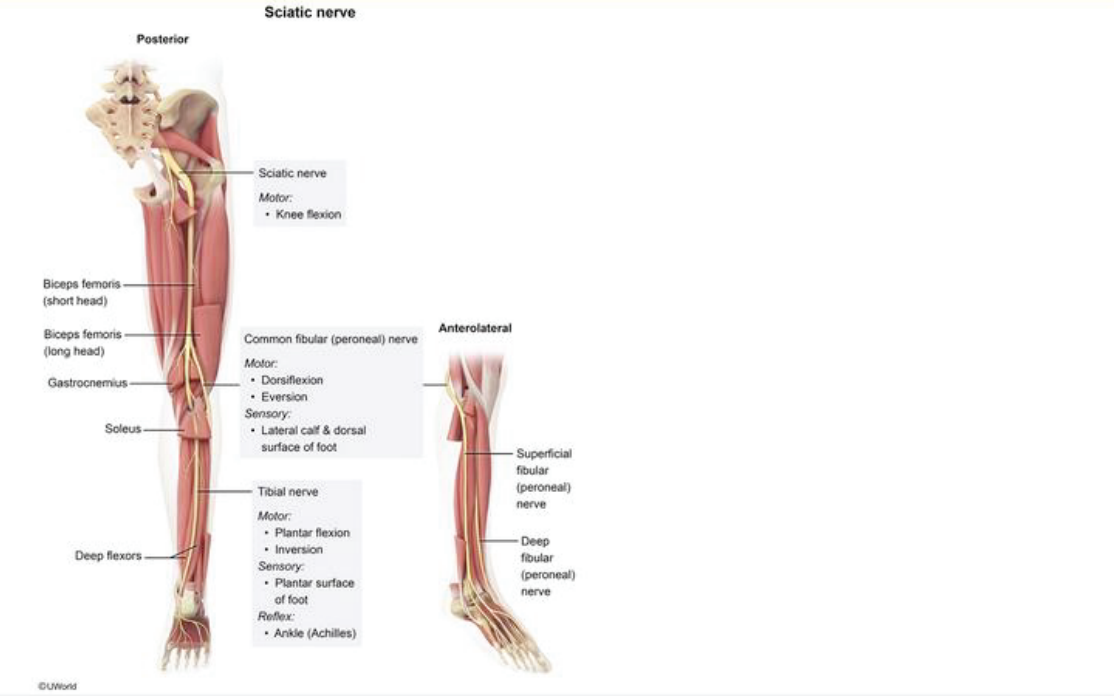


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The sciatic nerve branches into the **common fibular (peroneal) nerve** and the tibial nerve just proximal to the popliteal fossa. After coursing around the neck of the fibula, the common fibular nerve divides into deep and superficial branches. The deep branch innervates the anterior compartment muscles of the leg (foot and toe dorsiflexion) and provides sensation to the webspace between the first and second toes. The superficial branch innervates the lateral compartment muscles (foot eversion) and provides sensation to the dorsum of the foot and lateral shin.

The common fibular nerve is frequently injured by trauma (eg, lateral blows to the knee, tightly applied plaster casts) due to its superficial location at the **neck of the fibula**. Common fibular nerve injury can cause weakness on foot dorsiflexion (ie, **foot drop**) and eversion, as well as **impaired sensation** over the lateral shin and **dorsal foot** and between the first and second toes.

**(Choice A)** Compartment syndrome can occur with fracture/casting of the extremities because increased pressure in a confined space can compromise blood flow. Patients initially have severe pain out of proportion to the degree of injury, followed by weakness and sensory loss. Anterior compartment syndrome can injure the deep branch of the fibular nerve, causing impaired foot dorsiflexion and sensory loss between the first and second toes, but it would not affect foot eversion or sensation to the dorsal surface of the foot.


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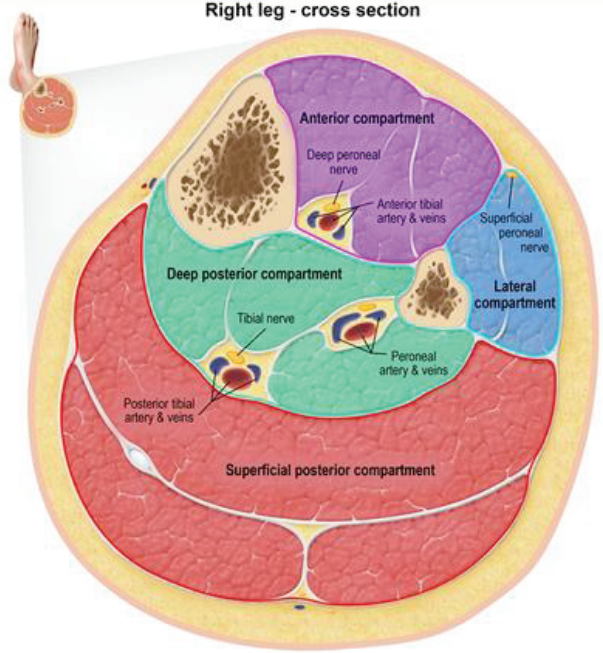
## Exhibit Display

Right leg - cross section

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surface of the foot.

**(Choice C)** Lateral compartment syndrome can injure the superficial branch of the fibular nerve, causing impaired foot eversion and sensory loss over the lateral shin and dorsum of the foot; weakness in foot dorsiflexion would not be expected.

**(Choices D and E)** After coursing through the popliteal fossa, the tibial nerve innervates the posterior compartment muscles of the leg. It then passes through the tarsal tunnel below the medial malleolus and provides sensory innervation over the sole and motor innervation to the intrinsic foot muscles. Tibial nerve injury at the popliteal fossa can cause weakness on foot plantar flexion, foot inversion, and toe flexion, whereas injury at the tarsal tunnel can cause sensory loss over the sole with intrinsic foot muscle weakness.

**Educational objective:**

Trauma/sustained pressure to the neck of the fibula can injure the common fibular nerve, causing weakness on foot dorsiflexion and eversion along with impaired sensation over the lateral shin, dorsal foot, and between the first and second toes.

**References**

- Evaluation and treatment of peroneal neuropathy.



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A 48-year-old woman comes to the office due to lower extremity discomfort. The patient reports no pain but describes an uncomfortable sensation in her legs, particularly in the evening and at night. The symptoms are relieved by leg movements or walking. She reports no behavioral or mood changes. The patient intermittently experiences mild migraines, and during a recent episode, antiemetic therapy worsened the leg discomfort. She has no other medical conditions and does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits, and physical examination shows no abnormalities. Blood cell counts, serum chemistry studies, and serum iron levels are within normal limits. Pharmacotherapy with which of the following mechanisms of action is most likely to relieve this patient's symptoms?

A. Beta-adrenergic antagonist
B. Dopamine receptor agonist
C. Muscarinic receptor antagonist
D. Opioid mu-receptor agonist
E. Selective serotonin reuptake inhibitor


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but describes an uncomfortable sensation in her legs, particularly in the evening and at night. The symptoms are relieved by leg movements or walking. She reports no behavioral or mood changes. The patient intermittently experiences mild migraines, and during a recent episode, antiemetic therapy worsened the leg discomfort. She has no other medical conditions and does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits, and physical examination shows no abnormalities. Blood cell counts, serum chemistry studies, and serum iron levels are within normal limits. Pharmacotherapy with which of the following mechanisms of action is most likely to relieve this patient's symptoms?

A. Beta-adrenergic antagonist (9%)

B. Dopamine receptor agonist (57%)

C. ~~Muscarinic receptor antagonist~~ (7%)

D. ~~Opioid mu-receptor agonist~~ (4%)

E. Selective serotonin reuptake inhibitor (20%)

Correct

57%

01 min, 43 secs

09/22/2020



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| Restless leg syndrome | |
|---|---|
| Clinical features | Uncomfortable urge to move the legs with:<br>• Unpleasant sensations in the legs<br>• Onset with inactivity or at night<br>• Relief with movement (eg, walking, stretching) |
| Causes | • Idiopathic<br>• Iron deficiency<br>• Uremia<br>• Diabetes (especially with neuropathy) |
| Treatment | • Avoidance of aggravating factors (eg, alcohol, sleep deprivation)<br>• Dopamine agonists (eg, pramipexole)<br>• Gabapentin/pregabalin |

This patient with vague lower extremity discomfort and an urge to move the legs that worsens at night has typical features of **restless legs syndrome (RLS)**. RLS is characterized by **uncomfortable sensations in**


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• Gabapentin/pregabalin

This patient with vague lower extremity discomfort and an urge to move the legs that worsens at night has typical features of **restless legs syndrome (RLS)**. RLS is characterized by **uncomfortable sensations in the legs** that are often difficult to describe and associated with an **urge to move** the lower extremities. Symptoms are **relieved with movement** (eg, walking, stretching) and are typically worse at **night**. As a result, patients often develop sleep-onset insomnia.

The pathophysiology of RLS is incompletely understood but likely involves **CNS iron deficiency** (even in patients with normal serum iron levels) and **abnormalities in dopaminergic transmission**. Certain medications, including dopamine antagonists (eg, antipsychotics, certain antiemetics [metoclopramide]), first-generation antihistamines (eg, diphenhydramine), and antidepressants (eg, selective serotonin reuptake inhibitors, mirtazapine) are associated with worsening symptoms **(Choice E)**.

Treatment includes avoidance of aggravating medications, **iron replacement**, and **dopamine agonists** (eg, ropinirole, pramipexole) which are thought to modulate CNS dopaminergic transmission and are rapidly effective in most cases.

**(Choice A)** Beta-adrenergic antagonists (eg, propranolol) are used for treating akathisia (ie, a strong urge to move), which occurs most commonly as a side effect of dopamine antagonists (eg, antipsychotic drugs).



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**(Choice A)** Beta-adrenergic antagonists (eg, propranolol) are used for treating akathisia (ie, a strong urge to move), which occurs most commonly as a side effect of dopamine antagonists (eg, antipsychotic drugs). However, akathisia is not accompanied by an unpleasant sensation in the legs and does not follow a circadian rhythm.

**(Choice C)** Muscarinic antagonists (eg, benztropine) have been used for the treatment of dystonia, which is characterized by sustained muscle contractions usually associated with abnormal posturing (eg, torticollis).

**(Choice D)** Opioid mu-receptor agonists (eg, codeine) are occasionally used for treating refractory RLS, but carry significant risks (eg, sedation, abuse, respiratory depression).

**Educational objective:**
Restless legs syndrome is characterized by an uncomfortable sensation in the legs accompanied by an urge to move them; symptoms worsen with inactivity and at night and are temporarily relieved with movement. Dopamine agonists (eg, pramipexole, ropinirole) are the preferred therapy for persistent symptoms.

**References**


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An 8-year-old boy is brought to the office by his mother for a routine checkup. He was diagnosed with absence seizures a year ago and has been undergoing treatment with an appropriate antiepileptic agent. The mother says that the patient is doing well and has not had any seizures since starting the medication. His school performance has improved significantly, and he no longer gets in trouble for "staring off" in class. He eats a well-balanced diet and is at the 50th percentile for height and weight. Which of the following is the most likely mechanism of action of the medication used in this patient?

A. Binds to GABA receptors and increases the chloride current
B. Binds to synaptic vesicles to modulate neurotransmitter release
C. Decreases the calcium current in thalamic neurons
D. Decreases the sodium current in cortical neurons
E. Increases brain beta-hydroxybutyrate acid levels

Submit


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An 8-year-old boy is brought to the office by his mother for a routine checkup. He was diagnosed with absence seizures a year ago and has been undergoing treatment with an appropriate antiepileptic agent. The mother says that the patient is doing well and has not had any seizures since starting the medication. His school performance has improved significantly, and he no longer gets in trouble for "staring off" in class. He eats a well-balanced diet and is at the 50th percentile for height and weight. Which of the following is the most likely mechanism of action of the medication used in this patient?

A. Binds to GABA receptors and increases the chloride current (10%)
B. Binds to synaptic vesicles to modulate neurotransmitter release (4%)
C. Decreases the calcium current in thalamic neurons (67%)
D. Decreases the sodium current in cortical neurons (16%)
E. Increases brain beta-hydroxybutyrate acid levels (1%)

Correct

67% Answered correctly

53 secs Time Spent

10/01/2020 Last Updated



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| Mechanisms of common antiseizure drugs | |
|---|---|
| **Phenytoin** | Blocks $Na^+$ channels |
| **Carbamazepine** | |
| **Valproic acid** | Blocks $Na^+$ channels & ↑ GABA levels |
| **Benzodiazepine** | ↑ $GABA_A$ action |
| **Phenobarbital** | |
| **Levetiracetam** | Modulates GABA & glutamate release |
| **Ethosuximide** | Blocks thalamic T-type $Ca^{2+}$ channels |

**Ethosuximide** is the first-line treatment for **absence seizures**. This drug **blocks T-type $Ca^{2+}$ channels** that trigger and sustain rhythmical burst discharges in **thalamic neurons**. Side effects of this drug are minimal and include nausea, vomiting, fatigue, and hyperactivity. If ethosuximide is not tolerated due to these side effects, or if the drug is ineffective in suppressing seizure activity, valproic acid is used as a second-line treatment for absence epilepsy. Valproic acid is a broad-spectrum antiseizure drug that inhibits voltage-dependent $Na^+$ channels and also causes a rise in GABA concentration.


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voltage-dependent $Na^+$ channels and also causes a rise in GABA concentration.

**(Choice A)** Benzodiazepines and barbiturates (eg, phenobarbital) bind to GABA receptors and allow an increased chloride current through the ion channel. This hyperpolarizes the cell membrane, which increases the threshold of excitability of the postsynaptic neuron.

**(Choice B)** Levetiracetam binds to a synaptic vesicle protein (SV2A) to modulate the release of GABA and glutamate neurotransmitters.

**(Choice D)** Phenytoin decreases the sodium current in cortical neurons by reducing the ability of sodium channels to recover from inactivation. This increases the refractory period of the neuron, inhibiting neuronal high-frequency firing. Carbamazepine and valproic acid have similar mechanisms of action.

**(Choice E)** Increasing the levels of brain beta-hydroxybutyrate acid (ketone bodies) is the goal of the ketogenic diet. This high-fat, low-carbohydrate diet may benefit some patients with refractory epilepsy.

**Educational objective:**
Ethosuximide, the first-line treatment for absence seizures, prevents neuronal burst firing by blocking thalamic T-type $Ca^{2+}$ channels. Phenytoin, carbamazepine, and valproic acid inhibit neuronal high-frequency firing by reducing the ability of $Na^+$ channels to recover from inactivation.


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A 54-year-old man is brought to the office by his daughter. She says that her father has been acting strangely over the past 2 years. He makes inappropriate sexual jokes, has little regard for social rules, is often irritable, and is borderline aggressive at times. The patient denies that his personality is any different from normal. When speaking with the patient, the physician notices that he has minimal verbal output and repeats "it is what it is" when asked questions about his strange behavior. On physical examination, he appears unkempt but otherwise has no significant findings. This patient most likely has a condition that predominantly involves which of the following structures?

A. Anterior temporal and prefrontal cortices
B. Caudate nucleus and putamen
C. Locus ceruleus and substantia nigra
D. Mamillary bodies and medial thalamus
E. Medial temporal and parietal cortices
F. Parietal and occipital cortices


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strangely over the past 2 years. He makes inappropriate sexual jokes, has little regard for social rules, is often irritable, and is borderline aggressive at times. The patient denies that his personality is any different from normal. When speaking with the patient, the physician notices that he has minimal verbal output and repeats "it is what it is" when asked questions about his strange behavior. On physical examination, he appears unkempt but otherwise has no significant findings. This patient most likely has a condition that predominantly involves which of the following structures?

- A. Anterior temporal and prefrontal cortices (78%) ✓
- B. Caudate nucleus and putamen (7%) ✗
- C. Locus ceruleus and substantia nigra (1%)
- D. Mamillary bodies and medial thalamus (5%)
- E. Medial temporal and parietal cortices (6%)
- F. Parietal and occipital cortices (0%)

Incorrect
Correct answer

78%
Answered correctly

01 min, 34 secs
Time Spent

02/05/2021
Last Updated



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| Differential diagnosis of dementia subtypes | |
|---|---|
| **Alzheimer disease** | • Early, insidious short-term memory loss<br>• Language deficits & spatial disorientation<br>• Later personality changes |
| **Vascular dementia** | • Stepwise decline<br>• Early executive dysfunction<br>• Cerebral infarction &/or deep white matter changes on neuroimaging |
| **Frontotemporal dementia** | • Early personality changes<br>• Apathy, disinhibition & compulsive behavior |


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| | |
|---|---|
| | on neuroimaging |
| **Frontotemporal dementia** | • Early personality changes<br>• Apathy, disinhibition & compulsive behavior<br>• Frontotemporal atrophy on neuroimaging |
| **Dementia with Lewy bodies** | • Visual hallucinations<br>• Spontaneous parkinsonism<br>• Fluctuating cognition<br>• Rapid eye movement behavior disorder |
| **Normal pressure hydrocephalus** | • Ataxia early in disease<br>• Urinary incontinence<br>• Dilated ventricles on neuroimaging |
| | • Behavioral changes |



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| | |
|---|---|
| **Prion disease** | • Behavioral changes<br>• Rapid progression<br>• Myoclonus &/or seizures |

This patient's **personality and behavioral changes** (eg, disinhibition, apathy, social inappropriateness, compulsive behaviors) and altered speech patterns (eg, paucity of speech, repeated phrases) are consistent with a diagnosis of behavioral variant **frontotemporal dementia** (FTD). Personality and behavioral changes present early in the disease course with neurocognitive deficits occurring later. FTD is highly heritable and a common cause of early-onset dementia.

FTD is characterized by initial **degeneration** of the prefrontal cortex that eventually progresses to include the anterior **temporal cortex**. Loss of function in the **prefrontal cortex** can cause inappropriate behavior, impaired judgment, and poor problem-solving skills (ie, executive dysfunction).

**(Choice B)** The caudate nucleus and putamen are basal ganglia structures that together form the dorsal striatum, which regulates voluntary movements. Huntington disease causes atrophy of the dorsal striatum (there is greater relative atrophy of the caudate) and presents with choreiform movements, psychiatric symptoms (eg, irritability, depression), and dementia. This patient's prominent personality changes and lack of a movement disorder are not characteristic of Huntington disease.


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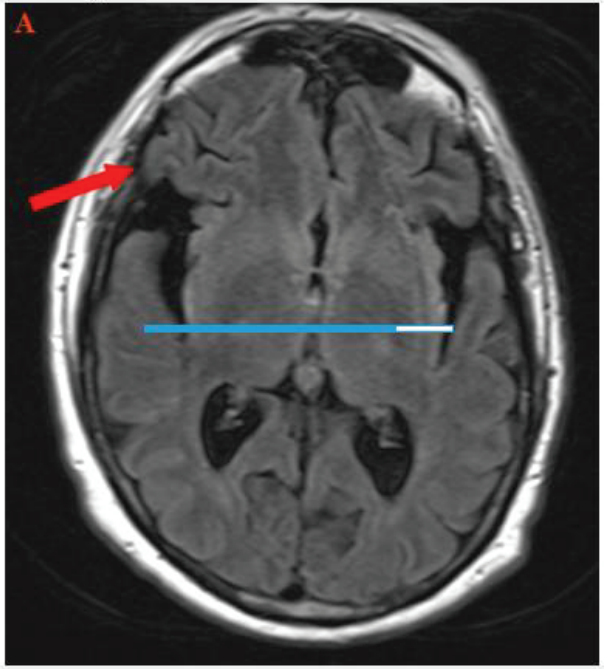
Frontotemporal lobar degeneration Frontotemporal lobar degeneration

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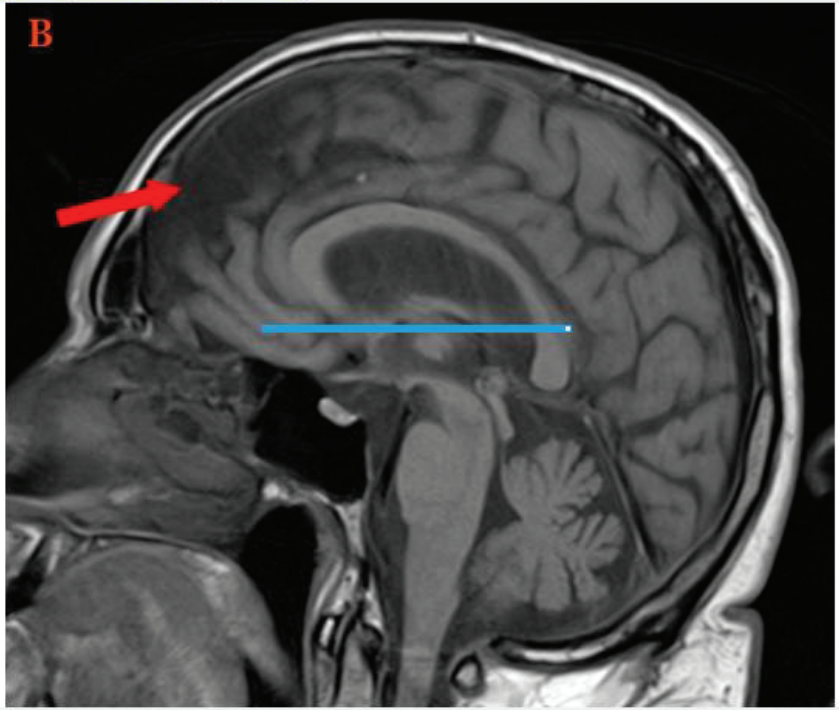
Frontotemporal lobar degeneration Frontotemporal lobar degeneration

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lack of a movement disorder are not characteristic of Huntington disease.

**(Choice C)** Neuronal loss in the locus ceruleus and substantia nigra is seen in Parkinson disease, which typically presents with tremor, bradykinesia, and rigidity. The locus ceruleus is a pontine structure that is one of the primary areas of norepinephrine synthesis in the brain. The substantia nigra, located in the midbrain, contains dopaminergic neurons whose axons project to the striatum (nigrostriatal pathway) and participate in regulation of voluntary movements.

**(Choice D)** Damage to the mammillary bodies and medial thalamus is characteristic of chronic Wernicke encephalopathy and Korsakoff syndrome. Both disorders result from chronic thiamine deficiency, most often in the context of heavy alcohol use.

**(Choice E)** Medial temporal and parietal cortical atrophy is characteristic of Alzheimer disease. The medial temporal lobe contains the hippocampus, a structure involved in the formation of new memories.

**(Choice F)** Disproportionate atrophy of the parietal and occipital cortices is seen in posterior cortical atrophy, an atypical variant of Alzheimer disease with prominent visual symptoms.

**Educational objective:**
Frontotemporal dementia is associated with pronounced atrophy of the prefrontal cortex with later degeneration of the anterior temporal cortex. It manifests initially with changes in personality, social


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midbrain, contains dopaminergic neurons whose axons project to the striatum (nigrostriatal pathway) and participate in regulation of voluntary movements.

**(Choice D)** Damage to the mammillary bodies and medial thalamus is characteristic of chronic Wernicke encephalopathy and Korsakoff syndrome. Both disorders result from chronic thiamine deficiency, most often in the context of heavy alcohol use.

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**(Choice F)** Disproportionate atrophy of the parietal and occipital cortices is seen in posterior cortical atrophy, an atypical variant of Alzheimer disease with prominent visual symptoms.

**Educational objective:**
Frontotemporal dementia is associated with pronounced atrophy of the prefrontal cortex with later degeneration of the anterior temporal cortex. It manifests initially with changes in personality, social behavior, and language that progress over time to a more global dementia with obvious neurocognitive deficits.

**References**

- Behavioural-variant frontotemporal dementia: diagnosis, clinical staging, and management.


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A 43-year-old woman says she cannot sleep due to pain and tingling affecting the first three digits of both hands. She has no problems with her legs. The patient suffers from chronic renal failure due to uncontrolled hypertension and receives hemodialysis. On examination, she has bilaterally diminished sensation over the thumb, index and middle fingers, and the radial half of her ring finger. Which of the following is the most likely mechanism of this patient's condition?

A. Endomysial inflammatory infiltration
B. Endoneural arteriole hyalinization
C. Endoneural multifocal demyelination
D. Mutations of a muscle structural protein gene
E. Nerve compression within an anatomic compartment

Submit



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A 43-year-old woman says she cannot sleep due to pain and tingling affecting the first three digits of both hands. She has no problems with her legs. The patient suffers from chronic renal failure due to uncontrolled hypertension and receives hemodialysis. On examination, she has bilaterally diminished sensation over the thumb, index and middle fingers, and the radial half of her ring finger. Which of the following is the most likely mechanism of this patient's condition?

- A. Endomysial inflammatory infiltration (4%)
- B. Endoneural arteriole hyalinization (24%)
- C. ~~Endoneural multifocal demyelination~~ (6%)
- D. ~~Mutations of a muscle structural protein gene~~ (0%)
- E. Nerve compression within an anatomic compartment (64%)

Incorrect
Correct answer
E

64%
Answered correctly

02 mins, 20 secs
Time Spent

01/16/2021
Last Updated



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Carpal tunnel, palmar view

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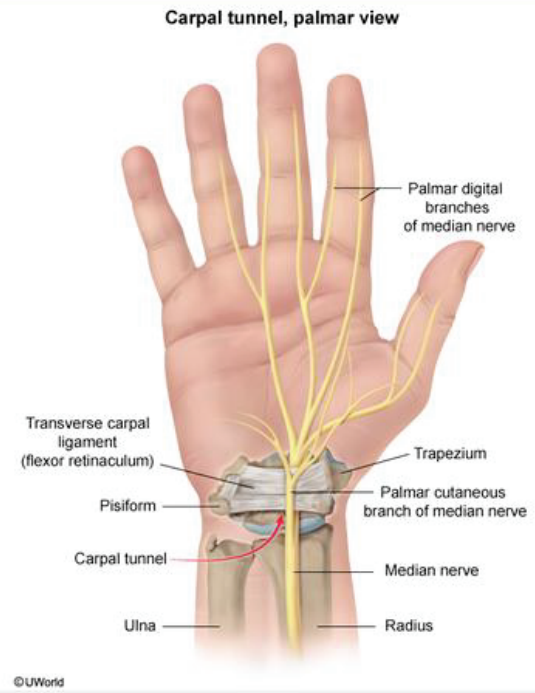


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**Carpal tunnel syndrome** (CTS) is a peripheral mononeuropathy caused by **compression** of the median nerve in the carpal tunnel. The carpal tunnel is an area located on the palmar surface of the wrist (between the carpal bones and transverse carpal ligament) in which the median nerve and tendons of the long flexors of the digits pass through. There is little room for expansion in this anatomical compartment.

CTS is associated with conditions that **reduce carpal tunnel space**, including pregnancy (fluid accumulation), hypothyroidism (glycosaminoglycan buildup), diabetes mellitus (connective tissue thickening), and rheumatoid arthritis (tendon inflammation). Patients with a long history of hemodialysis can also develop median nerve compression through deposition of β2-microglobulin (dialysis-associated amyloidosis) in the carpal tunnel.

Symptoms and signs of CTS often occur bilaterally and include:

1. Sensory impairment, pain, and/or paresthesias in the median nerve distribution (palmar surface of the first 3 digits and radial half of the 4th digit). Symptoms are usually worse at night.
2. Motor weakness during thumb abduction/opposition and **thenar atrophy**.
3. **Tinel sign** (tapping over the flexor surface of the wrist reproduces symptoms) and **Phalen sign**



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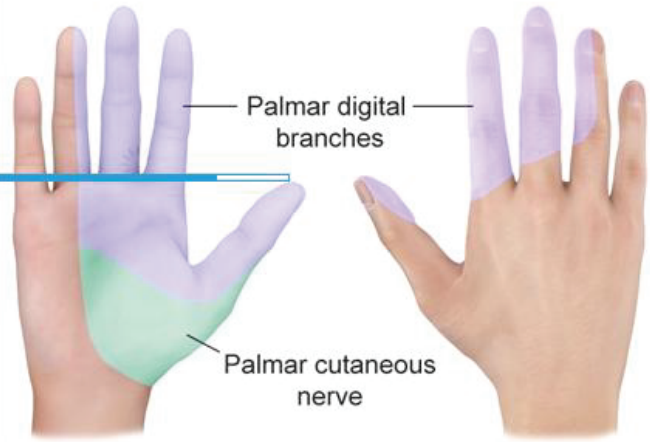
## Median nerve

| Motor function | Cutaneous innervation |
|---|---|
| • Thumb flexion & opposition<br>• Flexion of digits 2 & 3<br>• Wrist flexion & abduction<br>• Forearm pronation |  |

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1. Sensory impairment, pain, and/or paresthesias in the median nerve distribution (palmar surface of the first 3 digits and radial half of the 4th digit). Symptoms are usually worse at night.
2. Motor weakness during thumb abduction/opposition and **thenar atrophy**.
3. **Tinel sign** (tapping over the flexor surface of the wrist reproduces symptoms) and **Phalen sign** (flexion of the wrist reproduces symptoms).

**(Choice A)** Endomysial inflammatory infiltration is found on muscle biopsy in polymyositis, a myopathy that usually presents with proximal muscle weakness, not distal sensory symptoms as seen in this patient.

**(Choice B)** Endoneural arteriole hyalinization can occur in diabetes mellitus (diabetic microangiopathy) and most commonly results in a distal, symmetric peripheral polyneuropathy that usually starts in the feet. However, this patient does not have diabetes and her symptoms follow a median nerve distribution, which is more likely due to compressive neuropathy.

**(Choice C)** Endoneural inflammatory infiltration with multifocal demyelination is seen in Guillain-Barré syndrome, a demyelinating peripheral neuropathy that typically presents with ascending motor weakness. Patients with median nerve compression under the flexor retinaculum have focal, not multifocal, demyelination.

**(Choice D)** Duchenne muscular dystrophy is an X-linked condition that occurs due to mutation or deletion


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Patients with median nerve compression under the flexor retinaculum have focal, not multifocal, demyelination.

**(Choice D)** Duchenne muscular dystrophy is an X-linked condition that occurs due to mutation or deletion of the dystrophin gene. It is a myopathy that predominantly affects young boys and presents with proximal muscle weakness and pseudohypertrophy of the calves.

**Educational objective:**

Carpal tunnel syndrome is a peripheral neuropathy characterized by pain/paresthesias in a median nerve distribution (palmar surface of the first 3 digits and radial half of the 4th digit), weakness on thumb abduction/opposition, thenar atrophy, and a positive Tinel and/or Phalen test. It is caused by median nerve compression at the transverse carpal ligament.

**References**

- Carpal tunnel syndrome.

| Pathology | Nervous System | Carpal tunnel syndrome |
|---|---|---|
| Subject | System | Topic |

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www.ncbi.nlm.nih.gov/pubmed/21524035

A 13-year-old boy comes to the office for a postoperative follow-up visit. He was seen in the emergency department 3 weeks earlier with acute abdominal pain and was found to have acute appendicitis. The patient underwent urgent appendectomy without any apparent immediate complications and was released home. Several days later, he started having burning pain at the surgical scar radiating to the suprapubic region but otherwise feels well. Examination shows a healed surgical incision centered over McBurney point. There is a loss of sensation over the right suprapubic area. The cremasteric reflex is normal. Which of the following nerves is most likely injured in this patient?

A. Femoral
B. Genitofemoral
C. Iliohypogastric
D. Ilioinguinal
E. Lateral femoral cutaneous
F. Obturator



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department 3 weeks earlier with acute abdominal pain and was found to have acute appendicitis. The patient underwent urgent appendectomy without any apparent immediate complications and was released home. Several days later, he started having burning pain at the surgical scar radiating to the suprapubic region but otherwise feels well. Examination shows a healed surgical incision centered over McBurney point. There is a loss of sensation over the right suprapubic area. The cremasteric reflex is normal. Which of the following nerves is most likely injured in this patient?

- A. Femoral (1%)
- B. Genitofemoral (8%)
- ✓ C. Iliohypogastric (49%)
- D. Ilioinguinal (31%)
- E. Lateral femoral cutaneous (7%)
- F. Obturator (2%)

Correct

49%

57 secs

10/31/2020



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Abdominal and pelvic surgery can damage nerves innervating the abdominal wall skin and muscles due to transection from the incision, entrapment from fascia closure, or compression/stretching from tissue retraction or patient positioning. Transection may cause loss of skin sensation or muscle paralysis. Entrapment can cause burning/sharp pain due to continuous stimulation of pain fibers.

The iliohypogastric nerve arises from the L1 nerve root, emerges from the lateral border of the upper psoas major, and passes behind the kidney anterior to the quadratus lumborum. The nerve provides motor function to the anterolateral abdominal wall muscles. Its anterior branch emerges above the superficial inguinal ring to innervate the skin above the pubic region; the lateral branch descends over the iliac crest to innervate the gluteal region. Injury to the anterior branch during **appendectomy** causes decreased sensation at the suprapubic region.

**(Choice A)** The femoral nerve arises from the L2-L4 nerve roots. It provides sensation to the upper thigh and inner leg and innervates muscles that extend the knee.

**(Choice B)** The genitofemoral nerve arises from the L1-L2 nerve roots and provides sensation to the upper anterior thigh and motor function to parts of the genitalia (eg, cremasteric reflex in men, mons pubis in women).

**(Choice D)** The ilioinguinal nerve originates from the L1 nerve root and accompanies the spermatic cord



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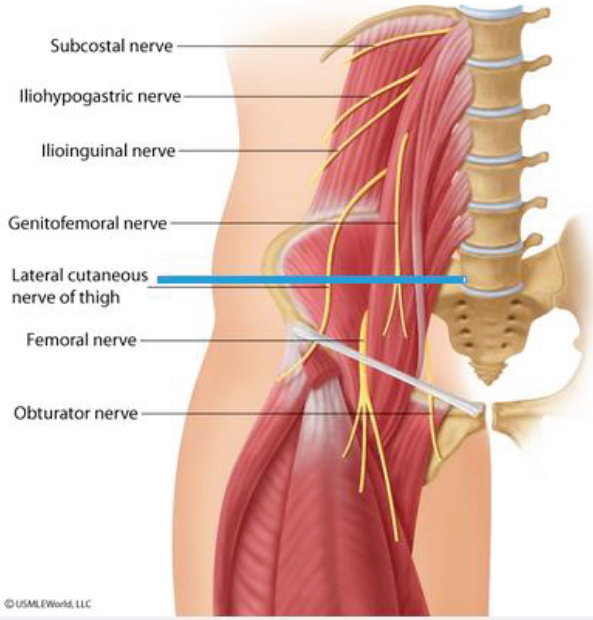
Major nerves of the lumbar plexus

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(Choice D) The ilioinguinal nerve originates from the L1 nerve root and accompanies the spermatic cord



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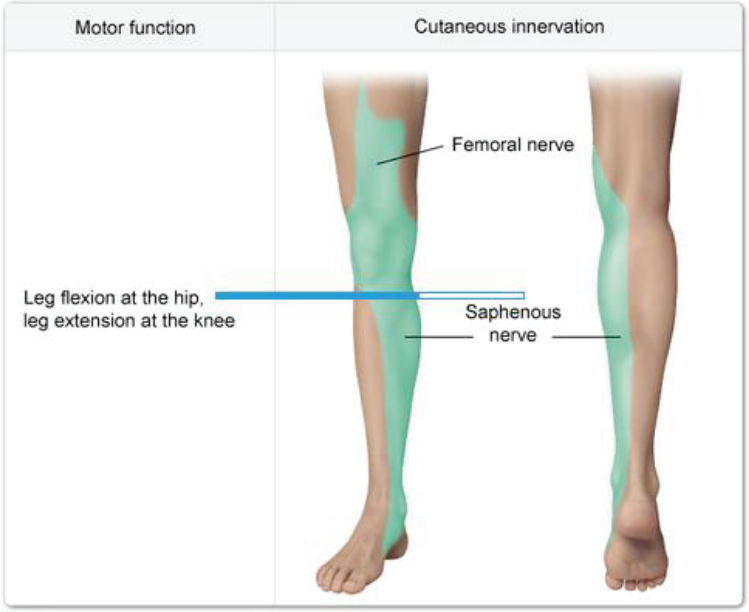
**Femoral nerve**

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(Choice D) The ilioinguinal nerve originates from the L1 nerve root and accompanies the spermatic cord



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upper anterior thigh and motor function to parts of the genitalia (eg, cremasteric reflex in men, mons pubis in women).

**(Choice D)** The ilioinguinal nerve originates from the L1 nerve root and accompanies the spermatic cord through the superficial inguinal ring. It provides sensation to the upper and medial thigh and parts of the external genitalia.

**(Choice E)** The lateral femoral cutaneous nerve arises from the L2-L3 nerve roots and provides sensation to the skin on the lateral thigh.

**(Choice F)** The obturator nerve arises from the L2-L4 nerve roots. It innervates the skin of the medial thigh and provides motor function for the adductor muscles of the lower extremity.

**Educational objective:**

The iliohypogastric nerve provides sensation to the suprapubic and gluteal regions and motor function to the anterolateral abdominal wall muscles. Abdominal surgery (eg, appendectomy) can damage the nerve and cause decreased sensation and/or burning pain at the suprapubic region.

**References**

- Abdominal wall paresis as a complication of laparoscopic surgery.



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upper anterior thigh and motor function to parts of the genitalia (eg, cremasteric reflex in men, mons pubis

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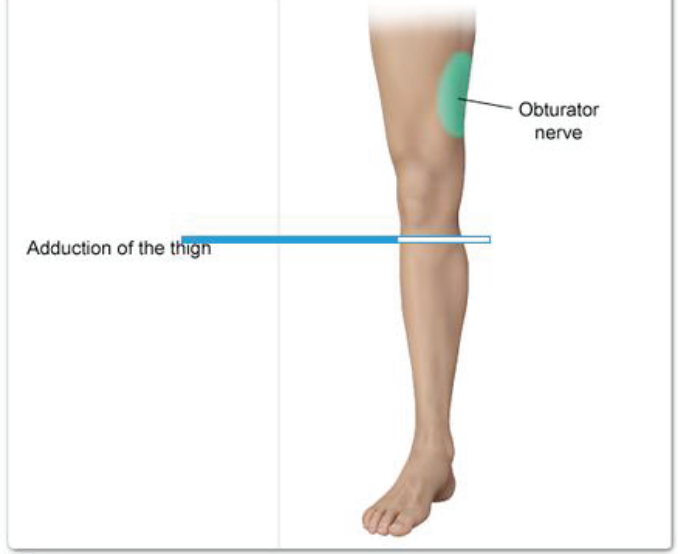
**Obturator nerve**

| Motor function | Cutaneous innervation |
|---|---|

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A 3-year-old girl is brought to the emergency department due to worsening fever and lethargy. Her parents report that she has had recurrent upper respiratory illness and recently had been irritable and pulling at her ears. She has also been eating poorly and vomiting, and has progressively become more lethargic. The patient has no chronic medical conditions and has received all recommended vaccinations. While being evaluated in the emergency department, she has a generalized tonic-clonic seizure. CT scan of the head shows a solitary 2-cm, ring-enhancing lesion in the left lateral temporal lobe. The pathogen responsible for this patient's current condition most likely gained access to the brain from which of the following structures?

A. Ethmoid air cells
B. Frontal sinus
C. Mastoid air cells
D. Maxillary sinus
E. Nose and upper lips
F. Peritonsillar space


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report that she has had recurrent upper respiratory illness and recently had been irritable and pulling at her ears. She has also been eating poorly and vomiting, and has progressively become more lethargic. The patient has no chronic medical conditions and has received all recommended vaccinations. While being evaluated in the emergency department, she has a generalized tonic-clonic seizure. CT scan of the head shows a solitary 2-cm, ring-enhancing lesion in the left lateral temporal lobe. The pathogen responsible for this patient's current condition most likely gained access to the brain from which of the following structures?

- A. Ethmoid air cells (18%)
- B. Frontal sinus (4%)
- ✓ C. Mastoid air cells (40%)
- D. Maxillary sinus (13%)
- E. Nose and upper lips (18%)
- F. Peritonsillar space (5%)

Correct

40%
Answered correctly

45 secs
Time Spent

01/20/2021
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**Brain abscess** is a contained area of liquefactive necrosis with a surrounding inflammatory capsule and marked vasogenic edema. It usually appears on imaging as a ring-enhancing lesion and often presents with headache, fever, and/or focal neurologic findings (eg, seizure). Most cases are **bacterial** in origin (eg, viridans streptococcus, *Staphylococcus aureus*) and stem from an underlying adjacent or distant infection.

The number and location of lesions helps differentiate the likely underlying source, as follows:

- **Single abscess** is usually due to the direct invasion of a contiguous infection. This patient who was pulling at her ears likely had otitis media that spread to the **mastoid air cells** and then invaded the adjacent temporal lobe leading to **temporal lobe abscess**. In contrast, frontal lobe abscess is generally due to direct spread of ethmoid or frontal sinusitis **(Choices A and B)**
- **Multiple abscesses** usually arise due to hematogenous dissemination of a distant infection, most commonly the heart (eg, endocarditis) or lungs (eg, abscess, empyema)

**(Choice D)** Maxillary sinusitis can spread contiguously to the orbit and cause periorbital or orbital cellulitis and abscess. Unlike the frontal and ethmoid sinus, the maxillary sinus is not adjacent to the brain.

(**Choice E)** Facial infections in the area around the eyes and nose drain into the opthalmic veins and can lead to cavernous sinus thrombosis, which usually presents with headache, fever, oculomotor deficits, and


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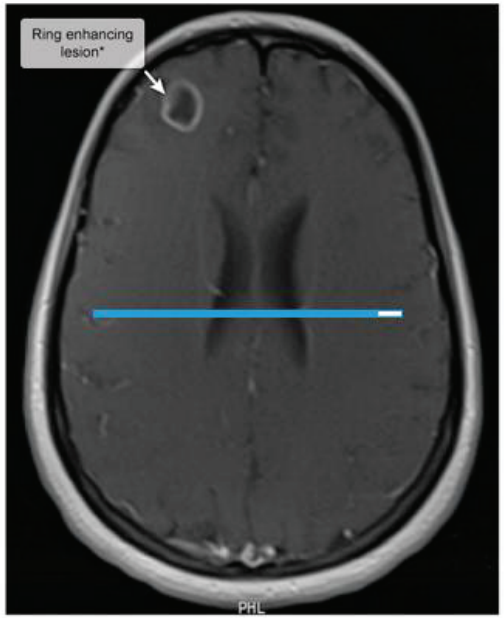
**Cerebral abscess**




*Liquefactive necrosis (dark) surrounded by a capsule

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**(Choice D)** Maxillary sinusitis can spread contiguously to the orbit and cause periorbital or orbital cellulitis and abscess. Unlike the frontal and ethmoid sinus, the maxillary sinus is not adjacent to the brain.

(**Choice E)** Facial infections in the area around the eyes and nose drain into the opthalmic veins and can lead to cavernous sinus thrombosis, which usually presents with headache, fever, oculomotor deficits, and eye swelling.

**(Choice F)** Peritonsillar abscess usually presents with fever, sore throat, and a muffled voice. Complications include airway obstruction and spread of the infection to the deep neck spaces or mediastinum.

**Educational objective:**
A single brain abscess is usually caused by direct spread of a contiguous infection. Temporal lobe abscess is usually a result of otitis media that has spread to the mastoid air cells, while frontal lobe abscess is usually due to ethmoid or frontal sinusitis. Multiple brain abscesses typically indicate hematogenous dissemination of a distant infection (eg, endocarditis, empyema).

| Anatomy | Nervous System | Brain abscess |
|---|---|---|
| Subject | System | Topic |



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A 32-year-old man is evaluated for bowel dysfunction. The patient suffered multiple injuries during a motor vehicle collision 6 months ago. He was hospitalized for several weeks and is currently undergoing treatment with physical therapy. Since the injury, the patient has developed severe constipation with occasional fecal incontinence. Evaluation reveals a large amount of stool in the distal colon due to impaired motor function. Anal sphincter tone is decreased. Injury to which of the following structures best explains this patient's bowel dysfunction?

- A. Cervical spinal cord
- B. Pudendal nerve
- C. Sacral spinal cord
- D. Thoracic spinal cord
- E. Vagus nerve nucleus

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A 32-year-old man is evaluated for bowel dysfunction. The patient suffered multiple injuries during a motor vehicle collision 6 months ago. He was hospitalized for several weeks and is currently undergoing treatment with physical therapy. Since the injury, the patient has developed severe constipation with occasional fecal incontinence. Evaluation reveals a large amount of stool in the distal colon due to impaired motor function. Anal sphincter tone is decreased. Injury to which of the following structures best explains this patient's bowel dysfunction?

- A. ~~Cervical spinal cord~~ (0%)
- B. ~~Pudendal nerve~~ (39%)
- ✓ C. Sacral spinal cord (52%)
- D. ~~Thoracic spinal cord~~ (2%)
- E. Vagus nerve nucleus (5%)

Correct

52% Answered correctly

01 min, 05 secs Time Spent

09/29/2020 Last Updated



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Answered correctly
Time Spent
Last Updated

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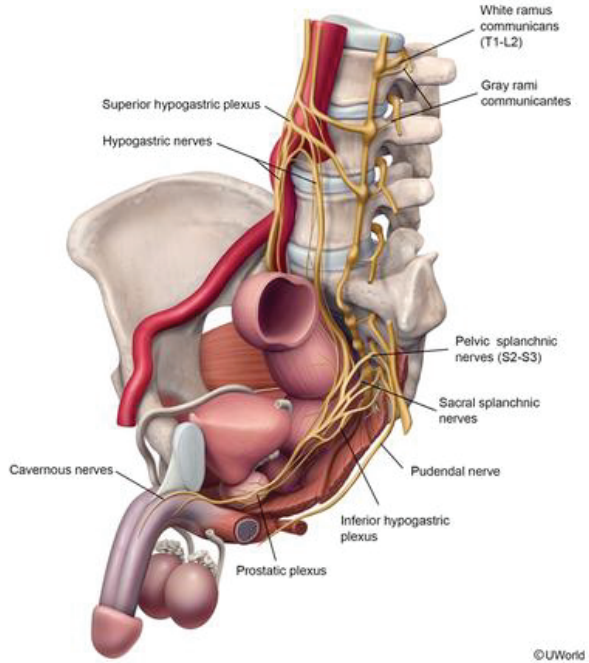
## Exhibit Display

### Pelvic autonomic nerves

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This patient has developed both constipation and fecal incontinence with decreased tone of the anal sphincter after traumatic injury.

A **deficiency of parasympathetic** input or **excess of sympathetic input** can lead to **constipation** by impairing peristalsis. Above the splenic flexure, peristalsis is controlled by parasympathetic innervation from the vagus nerve. Beyond the splenic flexure, it is controlled by **parasympathetic innervation** from the **S2-S4** nerve roots.

The innervation of the anal sphincter is complex and under voluntary, parasympathetic, and sympathetic control; therefore, **fecal incontinence** can occur due to lesions at multiple levels of the nervous system (eg, frontal cortex, spinal cord, peripheral nerves). The anal sphincter consists of an:

- **External sphincter**, which includes **skeletal muscle** and is under voluntary control innervated by the pudendal nerve (**S2-S4** branches)
- Internal sphincter, which includes smooth muscle that is contiguous with the rectum. Sympathetic innervation normally maintains it in a state of tonic contraction. Pressure in the rectal vault (due to the presence of stool) stimulates parasympathetic input from the pelvic splanchnic nerves to relax the sphincter.


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Therefore, this patient likely has **impairment** of both **parasympathetic and voluntary motor** output from the S2-S4 nerve roots because of **sacral spinal cord** (ie, conus medullaris) damage. This is leading to impaired peristalsis beyond the splenic flexure (ie, constipation) and flaccid weakness of the external anal sphincter (fecal incontinence).

**(Choices A and D)** Cervical or thoracic spinal cord injury could affect the upper motor neuron pathways involved in voluntary external anal sphincter function. However, this would lead to increased sphincter tone.

**(Choice B)** The pudendal nerve is involved in external anal sphincter innervation; dysfunction can lead to fecal incontinence. However, it does not provide parasympathetic innervation to the colon, so dysfunction would not lead to stool retention in the distal colon.

**(Choice E)** The vagus nerve (CN X) provides parasympathetic innervation to the GI tract above the colon's splenic flexure; injury classically causes delayed gastric emptying. However, distal colon stool retention is more likely related to impaired parasympathetic activity of the S2-S4 nerve roots. Also, vagal injury would not affect anal sphincter tone.

**Educational objective:**


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**(Choice B)** The pudendal nerve is involved in external anal sphincter innervation; dysfunction can lead to fecal incontinence. However, it does not provide parasympathetic innervation to the colon, so dysfunction would not lead to stool retention in the distal colon.

**(Choice E)** The vagus nerve (CN X) provides parasympathetic innervation to the GI tract above the colon's splenic flexure; injury classically causes delayed gastric emptying. However, distal colon stool retention is more likely related to impaired parasympathetic activity of the S2-S4 nerve roots. Also, vagal injury would not affect anal sphincter tone.

**Educational objective:**

Sacral spinal cord injury can lead to lower motor neuron injury of the S2-S4 nerve rootlets; these contribute parasympathetic innervation to the distal colon to stimulate peristalsis and voluntary motor innervation to the external anal sphincter. Lesions in this area can lead to distal colon stool retention, fecal incontinence, and a weak external anal sphincter.

**References**

- Central nervous system control of gastrointestinal motility and secretion and modulation of gastrointestinal functions.
- Control of motility in the internal anal sphincter.



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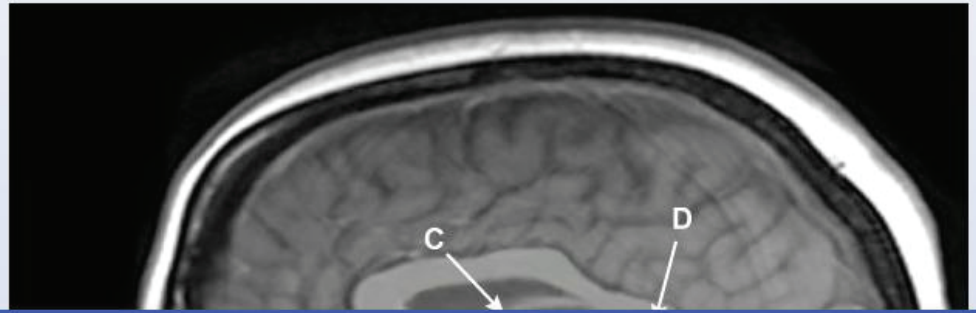
A 62-year-old man is brought to the office by his son due to memory impairment and frequent falls. The patient has been living alone since the death of his wife a year ago. His son, who is visiting from out of town, found his father in poor living conditions. The patient was forgetful and did not know the location of various items in his house, where he has lived for more than 20 years. His gait is also unsteady, and he had had several falls. The son says his father has always been "a drinker" and may have been drinking more recently. The patient is indifferent to his son's concerns and says he feels fine. Vital signs are within normal limits. On physical examination, bilateral lateral gaze palsy and nystagmus are present. Muscle strength and deep tendon reflexes are normal, but the gait is ataxic. On memory testing, he recalls 0 out of 3 objects after 5 minutes. A lesion of which of the following labeled structures on a normal brain MRI is most specifically associated with this patient's current condition?





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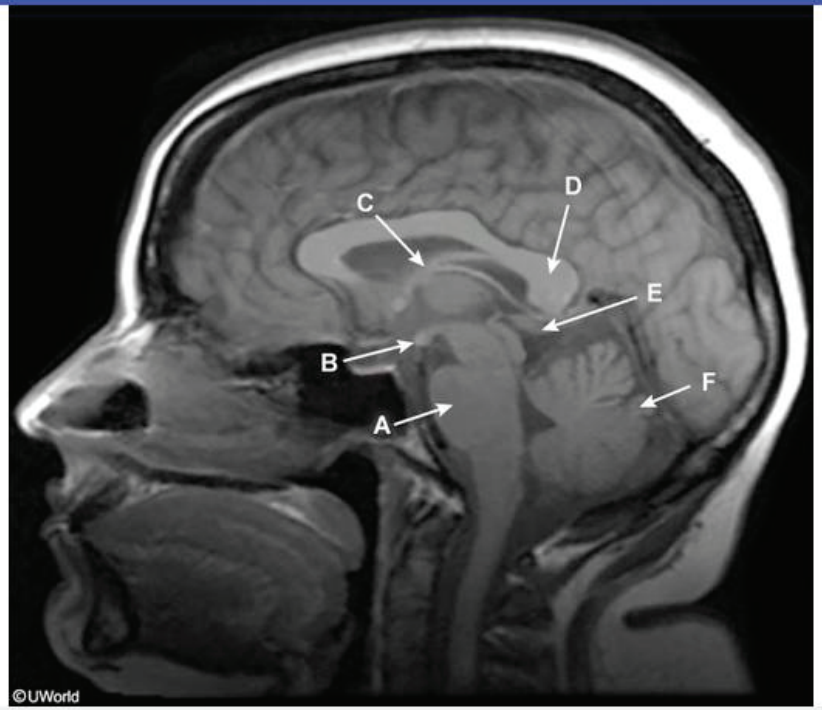


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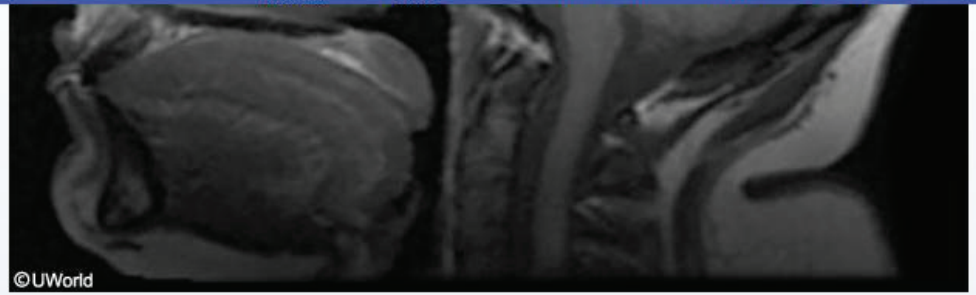


- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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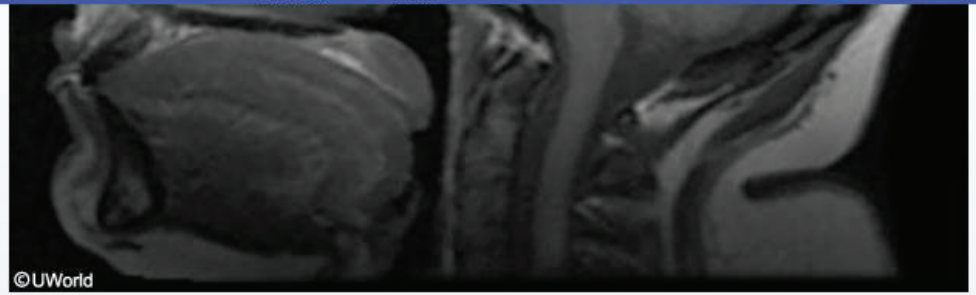


- A. A (4%)
- B. B (50%)
- C. C (8%)
- D. D (2%)
- E. E (16%)
- F. F (18%)

Correct

50%

02 mins, 54 secs

03/21/2021



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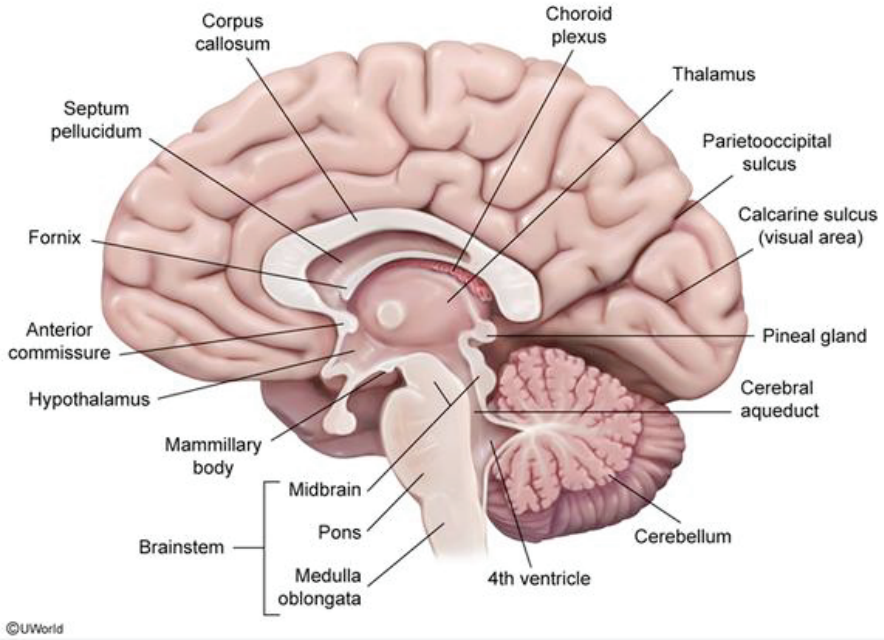
Median brain

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oblongata



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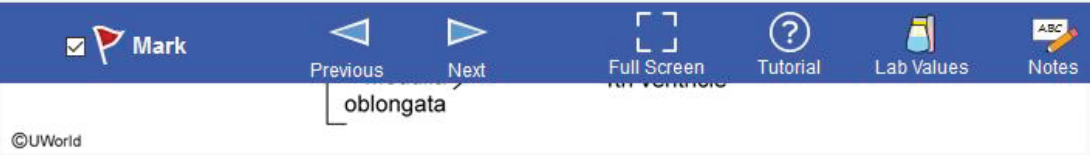


This patient with a suspected history of alcohol abuse has **oculomotor dysfunction** (nystagmus, ophthalmoplegia), **ataxia**, and **encephalopathy** (confusion, anterograde amnesia). This presentation is consistent with the classic triad of **Wernicke encephalopathy** (WE), a complication of thiamine (vitamin $B_1$) deficiency. **Thiamine** is a cofactor for multiple enzymes involved in glucose metabolism; deficiency results in the brain's inability to use glucose and turn it into energy, leading to neuronal damage and necrosis. Areas of the brain with high metabolic demand are particularly susceptible; the **mammillary bodies** are nearly universally affected and demonstrate focal hemorrhage or atrophy on imaging. Other commonly involved areas include the thalamus, periaqueductal gray substance, and locus caeruleus.

Thiamine deficiency occurs most commonly in patients with **chronic alcoholism** but can also manifest with any form of malnutrition (eg, anorexia, advanced malignancy). Infusion of dextrose-containing solutions without concurrent thiamine supplementation acutely lowers thiamine levels and can precipitate WE; however, some patients with severe deficiency can develop symptoms without a clear inciting event. The **chronic** effects of thiamine deficiency lead to **Korsakoff syndrome**, which is characterized by anterograde and retrograde amnesia, apathy, lack of insight, and confabulation. Attention, social behavior, and long-term memory are relatively preserved.



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term memory are relatively preserved.

**(Choice A)** Demyelination of the pons (central pontine myelinolysis) can occur with overly rapid correction of chronic hyponatremia. It can result in locked-in syndrome, in which patients can move their eyes but cannot move or verbally communicate. The pons is not typically involved in WE.

**(Choice C)** The fornix is a bundle of axons originating from the hippocampal subiculum that projects to the mammillary bodies. Although it can (rarely) be involved in WE, the mamillary bodies are more specifically associated.

**(Choice D)** The splenium of the corpus callosum is not typically affected in WE. Lesions (demyelinating or ischemic) in this structure will clinically result in alexia without agraphia.

**(Choice E)** The pineal gland synthesizes melatonin and is involved in circadian rhythm; it is not typically involved in WE.

**(Choice F)** Alcoholic cerebellar degeneration also causes ataxia but does not typically cause confusion or ophthalmoplegia. The cerebellum is less frequently involved in WE.

**Educational objective:**
Wernicke encephalopathy is a complication of thiamine deficiency and is characterized by oculomotor dysfunction, encephalopathy, and ataxia. Chronic deficiency results in Korsakoff syndrome (eg,



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associated.

**(Choice D)** The splenium of the corpus callosum is not typically affected in WE. Lesions (demyelinating or ischemic) in this structure will clinically result in alexia without agraphia.

**(Choice E)** The pineal gland synthesizes melatonin and is involved in circadian rhythm; it is not typically involved in WE.

**(Choice F)** Alcoholic cerebellar degeneration also causes ataxia but does not typically cause confusion or ophthalmoplegia. The cerebellum is less frequently involved in WE.

**Educational objective:**
Wernicke encephalopathy is a complication of thiamine deficiency and is characterized by oculomotor dysfunction, encephalopathy, and ataxia. Chronic deficiency results in Korsakoff syndrome (eg, anterograde and retrograde amnesia, confabulation, apathy). Thiamine is involved in glucose metabolism, and areas of the brain with high metabolic demands are particularly susceptible; the mammillary bodies are most commonly affected.

| Anatomy | Nervous System | Wernicke korsakoff syndrome |
|---|---|---|
| Subject | System | Topic |


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A 28-year-old woman comes to the office due to right hand tremors for the past several weeks. The patient has difficulty performing daily activities and feels embarrassed in social gatherings. She has a history of the remitting-relapsing form of multiple sclerosis. There is no family history of tremors. On physical examination, no abnormal hand movement is observed at rest. When the patient is instructed to touch an object on the table, a coarse tremor is observed that gradually increases as the hand moves closer to its target. Dysfunction of which of the following structures is the most likely cause of this patient's tremor?

A. Basal ganglia
B. Cerebellum
C. Motor cortex
D. Premotor cortex
E. Thalamus

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A. Basal ganglia (24%)
B. Cerebellum (62%)
C. Motor cortex (4%)
D. Premotor cortex (5%)
E. Thalamus (4%)

Correct

62%
Answered correctly

46 secs
Time Spent

01/08/2021
Last Updated



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| Tremor | Clinical features |
|---|---|
| **Essential** | • Action tremor<br>• Bilateral hands &/or head<br>• Improves with alcohol |
| **Parkinson disease** | • Resting tremor (decreases with movement)<br>• Hands & legs<br>• "Pill-rolling"<br>• Associated parkinsonian features (eg, rigidity, masked faces, wide-based gait) |
| **Cerebellar** | • Action tremor (increases as hand reaches target)<br>• Associated ataxia, dysmetria, or gait disorder |
| **Physiologic** | • Action & rest tremor<br>• Low amplitude, high frequency (ie, "fine" tremor)<br>• Not visible under normal circumstances<br>• Enhanced with sympathetic activation (eg, anxiety, caffeine, hyperthyroidism) |


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This patient has developed a large-amplitude (ie, coarse) tremor that worsens as the hand approaches the target, suggesting a cerebellar tremor. Cerebellar tremor can result from multiple pathologies that affect the cerebellum, most commonly **multiple sclerosis**, as in this patient. Other common causes include stroke, fragile X syndrome, and cerebellar degeneration.

Tremors due to cerebellar lesions are classically **low frequency** (ie, "slow," <5 Hz) and **high amplitude** (ie, coarse) because they involve the proximal, as well as the distal, muscles. The tremor classically increases in amplitude as an action approaches a target (ie, **intention tremor**). It is often accompanied by other **cerebellar signs**, including ataxia, dysmetria, and/or impaired rapidly alternating movements.

**(Choice A)** Parkinson disease occurs due to loss of dopaminergic neurons in the basal ganglia (substantia nigra). In contrast to this patient, patients with Parkinson disease classically have a resting tremor that improves with intentional movement. In addition, tremor would be accompanied by rigidity (increased resistance to passive movements), bradykinesia (slowing of voluntary movements), and gait disturbances.

**(Choice C)** The motor cortex controls voluntary muscle activity. Damage to this area causes a combination of spastic paralysis, clasp-knife rigidity, hyperreflexia, and pathologic reflexes but does not typically cause a rhythmic tremor.


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**(Choice C)** The motor cortex controls voluntary muscle activity. Damage to this area causes a combination of spastic paralysis, clasp-knife rigidity, hyperreflexia, and pathologic reflexes but does not typically cause a rhythmic tremor.

**(Choice D)** The premotor frontal cortex is responsible for the selection of movements in response to internal and external cues. A lesion affecting this part of the brain can result in abnormal posturing or repetitive movements but not an action tremor.

**(Choice E)** Lesions affecting the thalamus typically result in contralateral hemiplegia or contralateral hemisensory loss rather than tremor.

**Educational objective:**
Cerebellar tremors are classically low frequency (<5 Hz) and high amplitude and increase as an action approaches a target. They are often accompanied by other cerebellar signs, including ataxia, dysmetria, and impaired rapidly alternating movements.

| Anatomy | Nervous System | Tremor |
|---|---|---|
| Subject | System | Topic |

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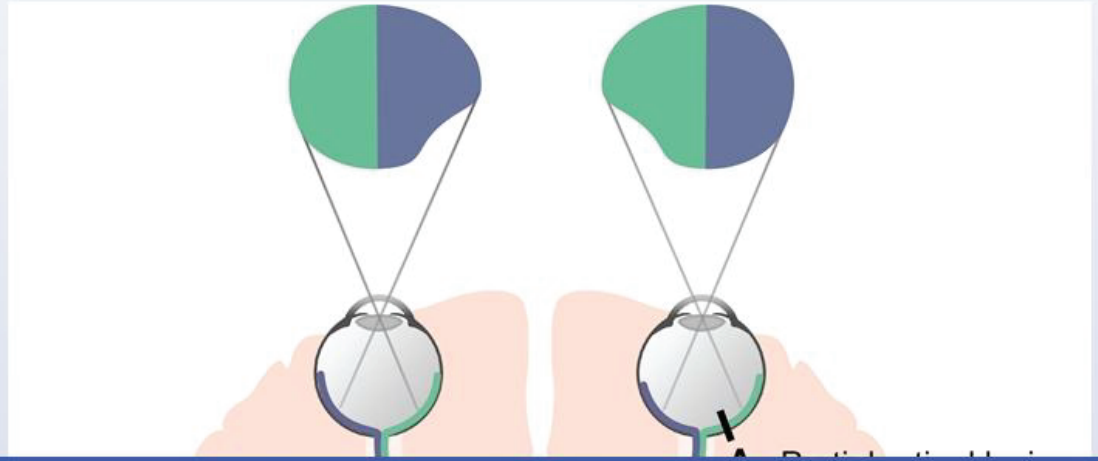
A 67-year-old woman comes to the clinic due to decreased vision in her right eye that she noticed a week ago. The patient says that her sight in the right eye is "narrower" than in the left. Her past medical history is significant for hypertension, type 2 diabetes mellitus, and hyperlipidemia. She also suffers from intermittent lower limb claudication and has had 2 prior episodes of transient vision loss in her right eye. Visual field testing reveals a right nasal hemianopia. MRI/magnetic resonance angiography of the head and neck reveal a right internal carotid artery aneurysm. Which of the following portions of the visual pathway is most likely disrupted in this patient?





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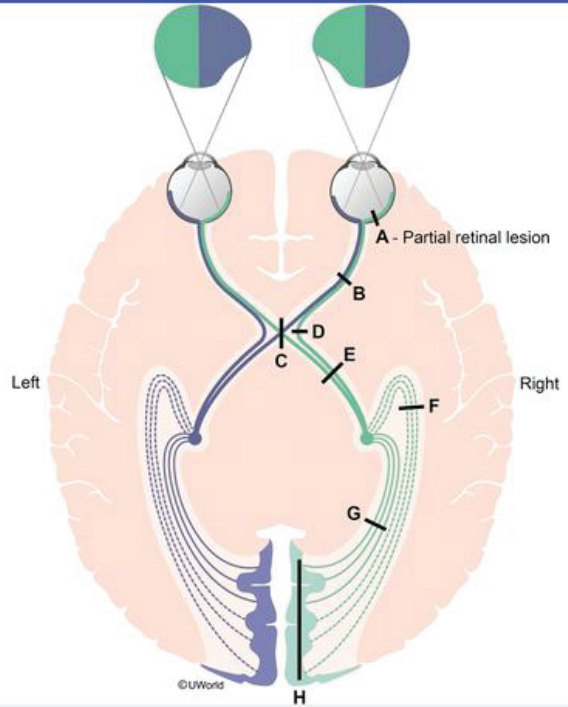


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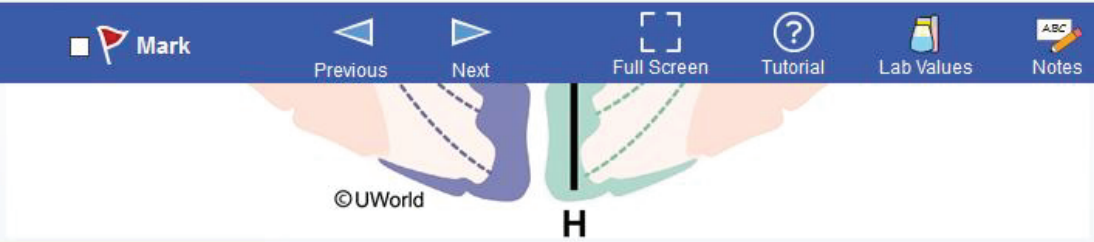


- A. A
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- E. E
- F. F
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- H. H

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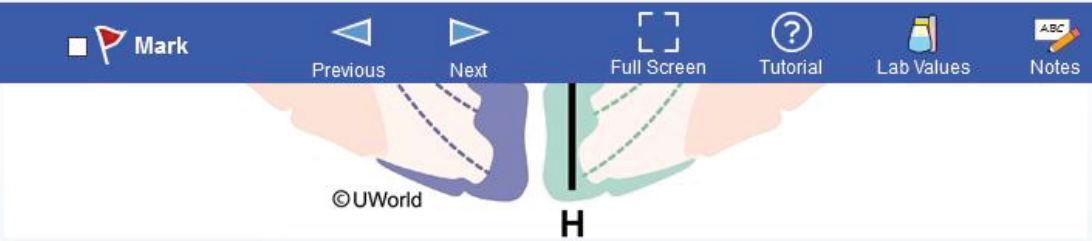


- A. A (27%)
- B. B (4%)
- C. C (1%)
- ✓ D. D (56%)
- E. E (4%)
- F. F (2%)
- G. G (0%)
- H. H (0%)

Correct

56%

02 mins, 12 secs

10/27/2020



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| Visual field defect | Location of lesion | Possible causes |
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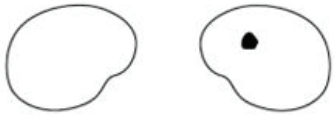
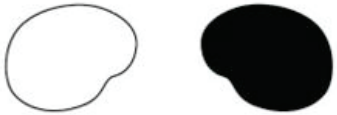
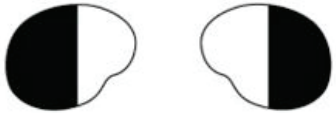
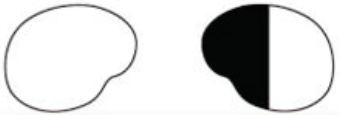
| A. Monocular scotoma  | Partial lesion in the retina, optic disc, optic nerve | Macular degeneration, optic neuritis |
| B. Right anopia  | Right optic nerve | Retinal artery or central retinal vein occlusion |
| C. Bitemporal hemianopia  | Optic chiasm | Pressure exerted by a pituitary tumor, craniopharyngioma, aneurysm of anterior communicating artery |
| D. Right nasal hemianopia  | Right peri-chiasmal lesion | Calcification or aneurysm of the internal carotid artery impinging on uncrossed, lateral retinal fibers |



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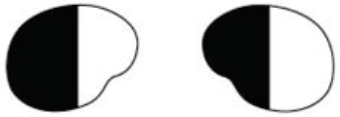
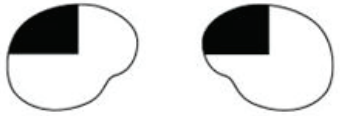
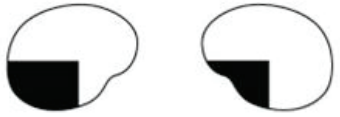
|---|---|---|
| E. Left homonymous hemianopia  | Right optic tract or optic radiation | Optic tract: occlusion of anterior choroidal artery<br>Optic radiation: occlusion of a middle cerebral artery branch or lesion involving posterior limb of internal capsule |
| F. Left homonymous superior quadrantanopia ("pie in the sky")  | Right temporal lobe (Meyer's loop) | Lesion or stroke involving temporal lobe |
| G. Left homonymous inferior quadrantanopia ("pie on the floor")  | Right parietal lobe (dorsal optic radiation) | Lesion or stroke involving parietal lobe |
| H. Left homonymous hemianopia | Right primary visual | Occlusion of posterior cerebral |



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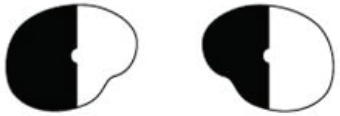
|---|---|---|
| H. Left homonymous hemianopia with macular sparing  | Right primary visual cortex (occipital lobe) | Occlusion of posterior cerebral artery. Macula is spared due to collateral blood from the middle cerebral artery |

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Humans have a maximum horizontal field of view of about 200 degrees with both eyes. The central 120 degrees make up the binocular field of view (stereoscopic vision), with 2 side fields of about 40 degrees seen by only 1 eye (monoscopic vision). Unilateral visual defects within the binocular field of view (such as unilateral nasal hemianopia) may be masked due to compensation by the normal eye and may go unnoticed by the patient.

Light from the nasal visual field strikes the temporal side of each retina, and optic nerve fibers from the temporal part of the retina travel laterally through the optic chiasm to pass into the ipsilateral optic tract. Lesions involving the **lateral** aspects of the **optic chiasm** can cause ipsilateral **nasal hemianopia** by damaging these uncrossed, temporal retinal fibers. This may occur with **aneurysm** of the **internal carotid artery** (eg, cavernous or ophthalmic segments), as seen in this patient.

**(Choice A)** A partial lesion involving the retina is more likely to produce focal monocular scotoma than


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H. Left homonymous hemianopia | Right primary visual | Occlusion of posterior cerebral

Exhibit Display

| Visual field defect | Location of lesion | Possible causes |
|---|---|---|
| A. Monocular scotoma | Partial lesion in the retina, optic disc, optic nerve | Macular degeneration, optic neuritis |
| B. Right anopia | Right optic nerve | Retinal artery or central retinal vein occlusion |
| C. Bitemporal hemianopia | Optic chiasm | Pressure exerted by a pituitary tumor, craniopharyngioma, aneurysm of anterior communicating artery |
| D. Right nasal hemianopia | Right peri-chiasmal lesion | Calcification or aneurysm of the internal carotid artery impinging on uncrossed, lateral retinal fibers |
| E. Left homonymous hemianopia | Right optic tract or optic radiation | Optic tract: occlusion of anterior choroidal artery<br>Optic radiation: occlusion of a middle cerebral artery branch or lesion involving posterior limb of internal capsule |
| F. Left homonymous superior quadrantanopia ("pie in the sky") | Right temporal lobe (Meyer's loop) | Lesion or stroke involving temporal lobe |
| G. Left homonymous inferior quadrantanopia ("pie on the floor") | Right parietal lobe (dorsal optic radiation) | Lesion or stroke involving parietal lobe |
| H. Left homonymous hemianopia with macular sparing | Right primary visual cortex (occipital lobe) | Occlusion of posterior cerebral artery. Macula is spared due to collateral blood from the middle cerebral artery |

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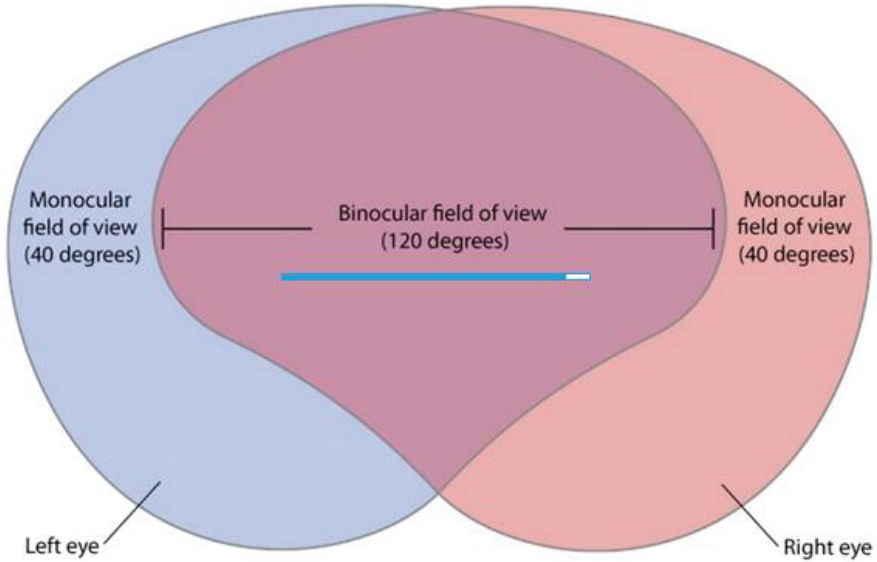
H. Left homonymous hemianopia | Right primary visual | Occlusion of posterior cerebral

Exhibit Display

Binocular visual field

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temporal part of the retina travel laterally through the optic chiasm to pass into the ipsilateral optic tract.

Lesions involving the **lateral** aspects of the **optic chiasm** can cause ipsilateral **nasal hemianopia** by damaging these uncrossed, temporal retinal fibers. This may occur with **aneurysm** of the **internal carotid artery** (eg, cavernous or ophthalmic segments), as seen in this patient.

**(Choice A)** A partial lesion involving the retina is more likely to produce focal monocular scotoma than nasal hemianopia as a lesion with the latter would need to involve the entire temporal hemiretina.

**Educational objective:**

An aneurysm of the internal carotid artery can laterally impinge on the optic chiasm. This can cause ipsilateral nasal hemianopia by damaging uncrossed optic nerve fibers from the temporal portion of the retina.

**References**

- Unilateral nasal hemianopia as a sign of intracranial optic nerve compression.
- Giant aneurysms of the carotid system presenting as visual field defect.

| Anatomy | Nervous System | Visual pathway |
|---|---|---|
| Subject | System | Topic |

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A 20-year-old man is evaluated in the clinic for right arm weakness and numbness. He is a competitive baseball pitcher and says that he played a lot more innings than usual last week because his team made the playoffs. Since then, the patient has had difficulty using the right arm, particularly when lifting objects. He has no known history of head, neck, or upper extremity trauma. On physical examination, there is diminished strength on right elbow flexion and an absent biceps reflex. This patient is most likely to have sensory loss over which of the following areas?

A. Lateral forearm
B. Medial forearm
C. Posterior arm
D. Posterior forearm
E. Thenar eminence

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A 20-year-old man is evaluated in the clinic for right arm weakness and numbness. He is a competitive baseball pitcher and says that he played a lot more innings than usual last week because his team made the playoffs. Since then, the patient has had difficulty using the right arm, particularly when lifting objects. He has no known history of head, neck, or upper extremity trauma. On physical examination, there is diminished strength on right elbow flexion and an absent biceps reflex. This patient is most likely to have sensory loss over which of the following areas?

- A. Lateral forearm (57%)
- B. Medial forearm (22%)
- C. Posterior arm (8%)
- D. Posterior forearm (4%)
- E. Thenar eminence (6%)

Correct

57%
Answered correctly

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Answered correctly
Time Spent
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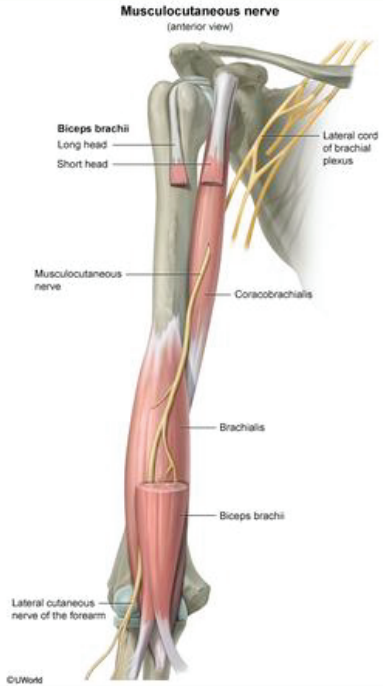


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This patient likely has musculocutaneous nerve injury, which most commonly occurs in the setting of trauma (eg, shoulder dislocation) and strenuous upper extremity activity (eg, baseball pitching). The musculocutaneous nerve is derived from the C5-C7 spinal nerve roots and arises from the lateral cord of the brachial plexus. It innervates the major **forearm flexors** (eg, biceps brachii, brachialis) and coracobrachialis (flexes and adducts the arm). After innervating these muscles, the remaining fibers become the lateral cutaneous nerve of the forearm and provide sensory innervation to the skin of the **lateral forearm**.

**(Choice B)** The medial forearm receives sensory innervation from a branch of the medial cord of the brachial plexus (medial cutaneous nerve of the forearm).

**(Choices C and D)** The posterior arm and forearm receive sensory innervation from the posterior cutaneous branches of the radial nerve.

**(Choice E)** The thenar eminence receives sensory innervation from the palmar cutaneous branch of the median nerve, which arises proximal to the carpal tunnel.

**Educational objective:**
The musculocutaneous nerve innervates the major forearm flexors (eg, biceps brachii, brachialis) and



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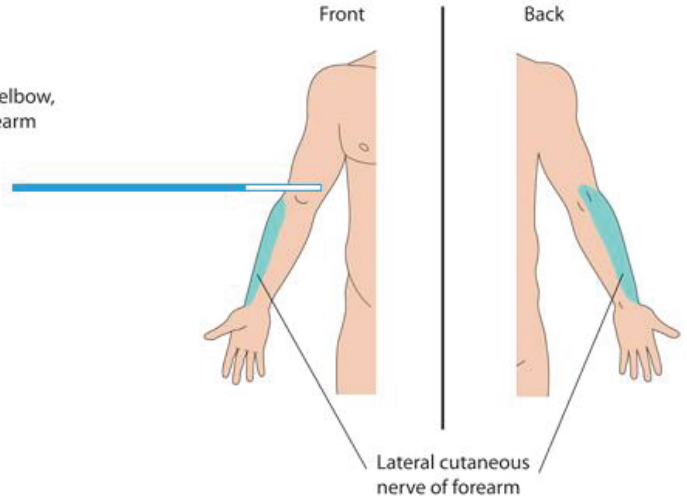
## Important nerves in the arm

| Nerve | Motor function | Region of sensory loss with neuropathy |
|---|---|---|
| Musculocutaneous nerve | Flexion of arm at elbow, supination of forearm | |

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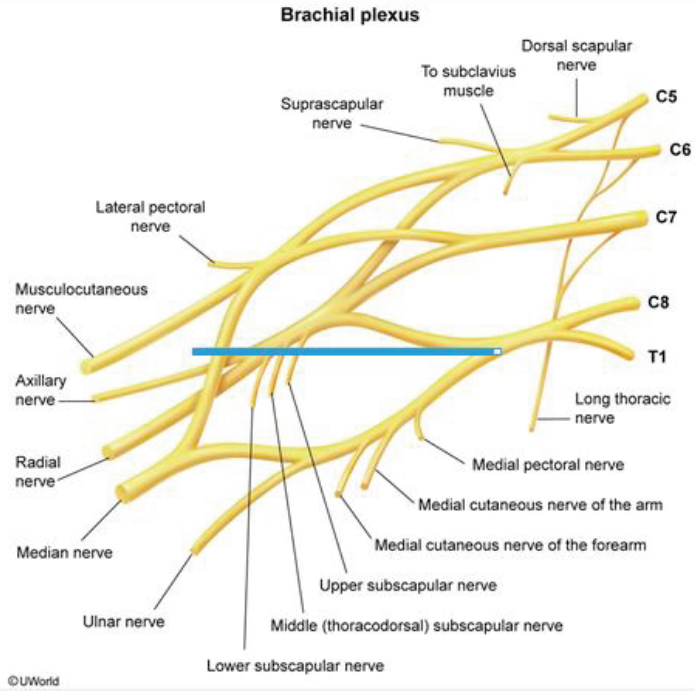


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become the lateral cutaneous nerve of the forearm and provide sensory innervation to the skin of the **lateral forearm**.

**(Choice B)** The medial forearm receives sensory innervation from a branch of the medial cord of the brachial plexus (medial cutaneous nerve of the forearm).

**(Choices C and D)** The posterior arm and forearm receive sensory innervation from the posterior cutaneous branches of the radial nerve.

**(Choice E)** The thenar eminence receives sensory innervation from the palmar cutaneous branch of the median nerve, which arises proximal to the carpal tunnel.

**Educational objective:**

The musculocutaneous nerve innervates the major forearm flexors (eg, biceps brachii, brachialis) and coracobrachialis (flexes and adducts the arm) and provides sensory innervation to the lateral forearm. It is derived from the upper trunk of the brachial plexus (C5-C7) and can be injured by trauma or strenuous upper extremity exercise.

**References**

- Peripheral nerve entrapment and injury in the upper extremity.
- Musculocutaneous neuropathy: case report and discussion



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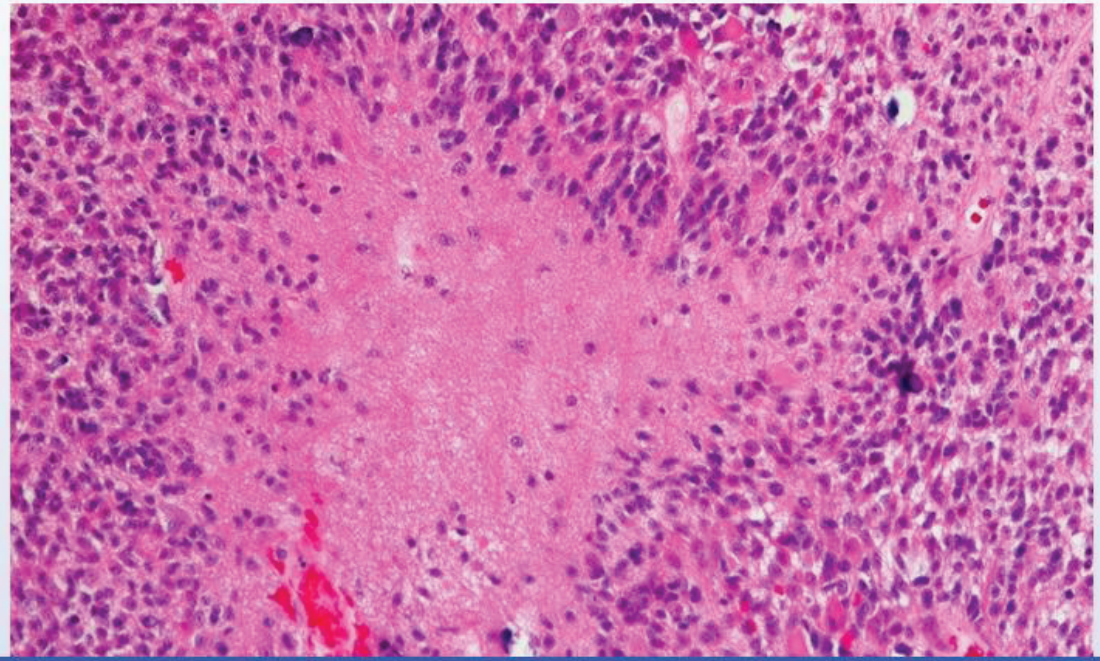
A 64-year-old man is being evaluated for nausea and a new-onset headache that worsens when he bends over. Brain imaging shows a hemispheric cerebral mass that is subsequently biopsied. Light microscopy of the tissue specimen is shown in the image below.





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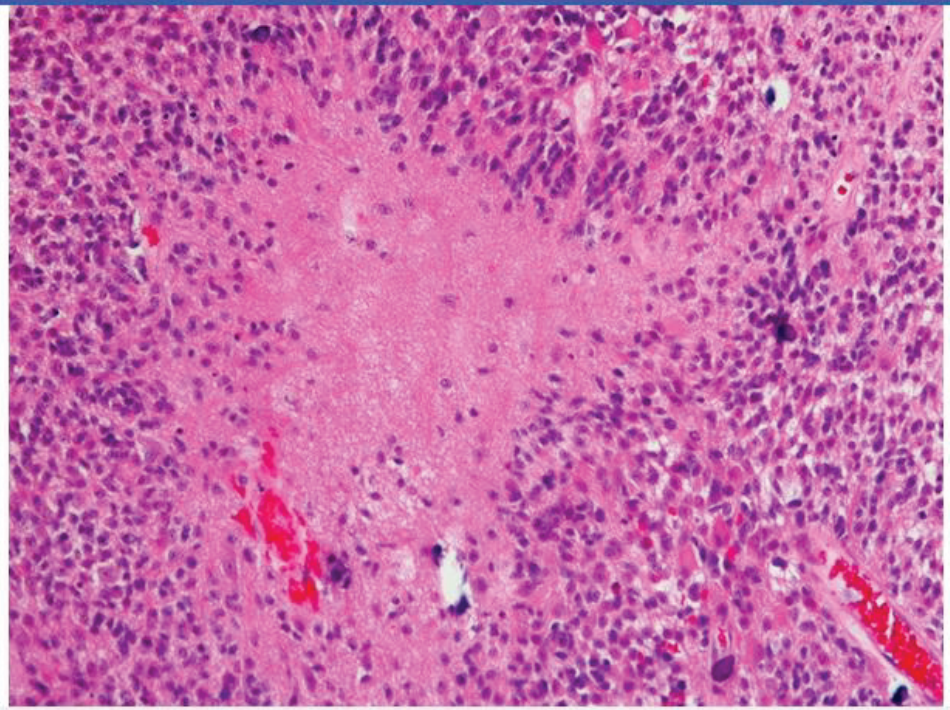

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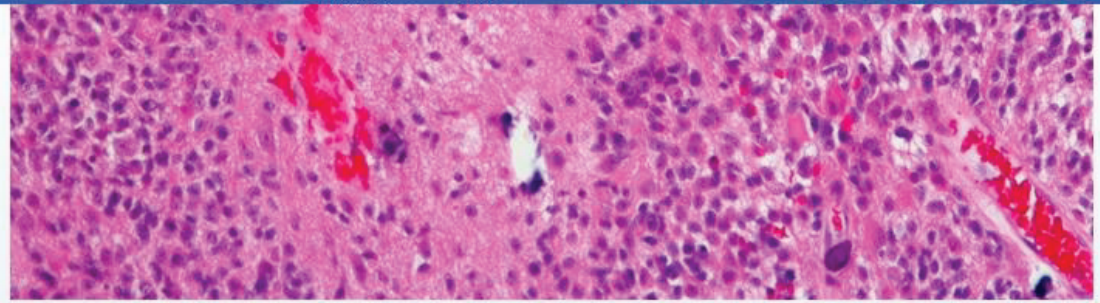

Which of the following histologic findings is most characteristic of this lesion?

A. Cyst formation and rare mitoses

B. Inflammatory cell infiltrate and reticulin deposits

C. Microscopic laminar calcium deposition

D. Necrosis and vascular proliferation

E. Proliferating cells surrounding blood vessels

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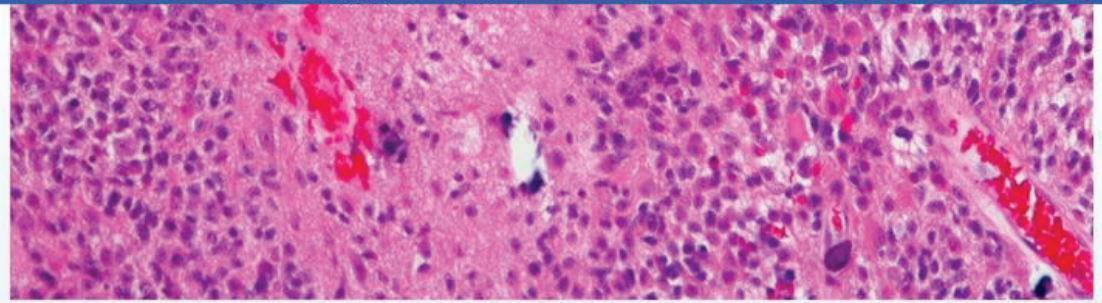

Which of the following histologic findings is most characteristic of this lesion?

A. ~~Cyst formation and rare mitoses~~ (3%)

✗ B. Inflammatory cell infiltrate and reticulin deposits (13%)

C. ~~Microscopic laminar calcium deposition~~ (3%)

✓ D. Necrosis and vascular proliferation (62%)

E. ~~Proliferating cells surrounding blood vessels~~ (17%)

Incorrect
Correct answer

62%

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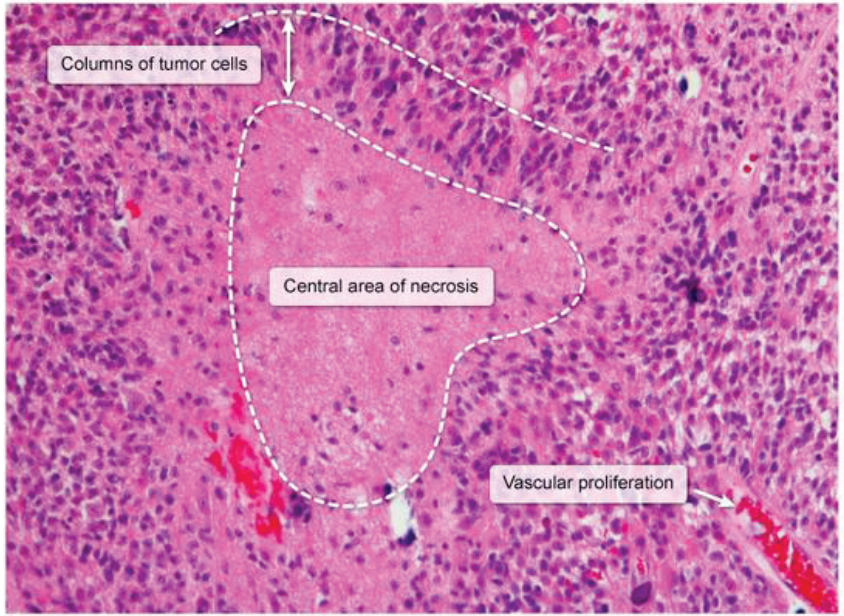
Glioblastoma multiforme

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This image shows an area of necrosis surrounded by columns of tumor cells (ie, **pseudopalisading necrosis**) with capillaries at the periphery (**vascular proliferation**). These histologic features are characteristic of glioblastoma multiforme (GBM), a malignant glioma that is the most common primary brain neoplasm in adults. GBM is usually located within the cerebral hemispheres (eg, frontal lobe, temporal lobe) and often presents with **new-onset headache** that worsens with bending over (increases intracranial pressure). Nausea/vomiting, focal neurological defects, and/or seizures are also frequently seen. The prognosis for patients with GBM is poor, with median survival at 10-12 months.

**(Choice A)** Cyst formation and rare mitoses indicate a colloid cyst, a pathologically benign tumor usually found in the third ventricle. Although colloid cysts are usually asymptomatic, they can cause lethal obstructive hydrocephalus.

**(Choice B)** Reticulin deposits and chronic inflammatory infiltrates are seen in pleomorphic xanthoastrocytomas. Although they can rarely progress to GBM, these tumors are usually found in children and young adults.

**(Choice C)** Meningiomas are tumors of the meninges that have a whorled pattern of growth. Although they are not always present, laminar calcifications called psammoma bodies are characteristic of benign meningiomas.


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This image shows a
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**(Choice A)** Cyst fo
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**(Choice B)** Reticu
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**(Choice C)** Menin
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Exhibit Display

| Glioblastoma multiforme | |
|---|---|
| **Onset** | Age 40-70 |
| **Cell of origin** | Astrocyte |
| **Location** | • Frontal & temporal lobes, basal ganglia<br>• Commonly **crosses the midline** (butterfly distribution) |
| **Macroscopic appearance** | • Areas of necrosis & hemorrhage (variegated appearance, thus termed multiforme)<br>• Poorly demarcated from surrounding tissue |
| **Microscopic appearance** | • **Pseudopalisading necrosis** (foci of necrosis surrounded by tumor cells)<br>• New vessel formation<br>• Small round cells, bizarre giant cells, large number of mitoses |
| **Symptoms** | • Headache<br>• Seizure<br>• Mental status change<br>• Focal neurologic symptoms |
| **Prognosis** | • Highly malignant |

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This image shows a
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| **Onset** | Age 40-70 |
| **Cell of origin** | Astrocyte |
| **Location** | • Frontal & temporal lobes, basal ganglia<br>• Commonly **crosses the midline** (butterfly distribution) |
| **Macroscopic appearance** | • Areas of necrosis & hemorrhage (variegated appearance, thus termed multiforme)<br>• Poorly demarcated from surrounding tissue |
| **Microscopic appearance** | • **Pseudopalisading necrosis** (foci of necrosis surrounded by tumor cells)<br>• New vessel formation<br>• Small round cells, bizarre giant cells, large number of mitoses |
| **Symptoms** | • Headache<br>• Seizure<br>• Mental status change<br>• Focal neurologic symptoms |
| **Prognosis** | • Highly malignant<br>• Death within 1 year of diagnosis |

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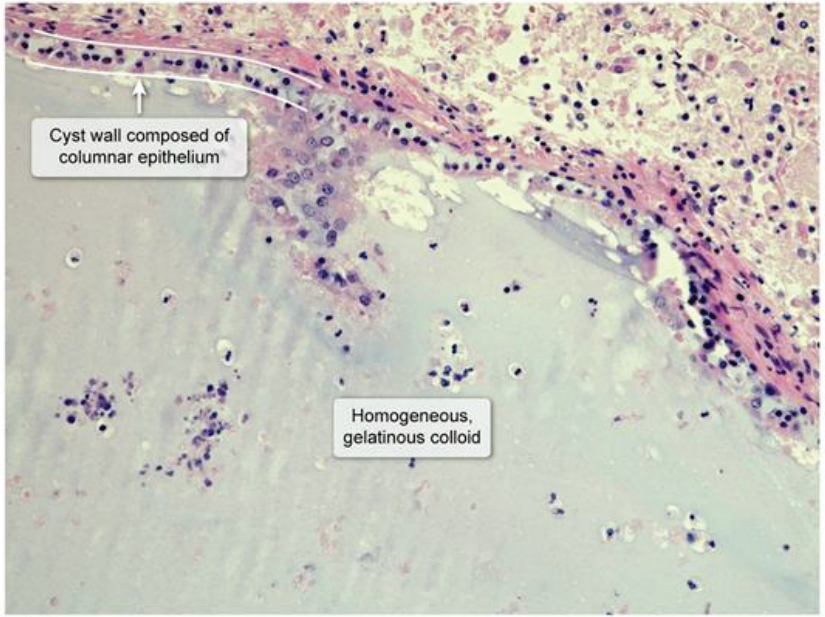
Colloid cyst of the third ventricle

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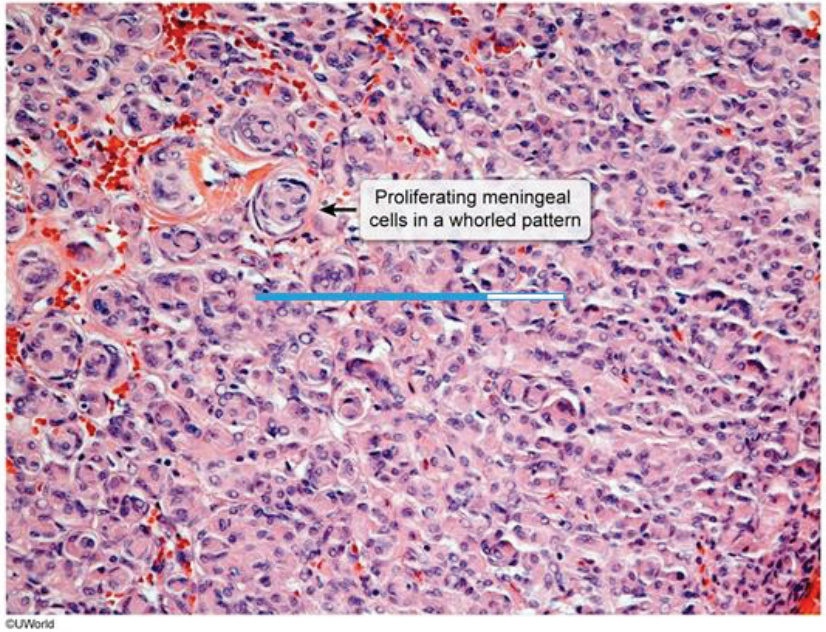
Meningioma

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xanthoastrocytomas. Although they can rarely progress to GBM, these tumors are usually found in children and young adults.

**(Choice C)** Meningiomas are tumors of the meninges that have a whorled pattern of growth. Although they are not always present, laminar calcifications called psammoma bodies are characteristic of benign meningiomas.

**(Choice E)** Ependymomas also display prominent vascular proliferation. However, these tumors are usually infratentorial (eg, fourth ventricle, spinal cord), rare in adults, and characterized histologically by proliferating ependymal cells surrounding blood vessels (perivascular pseudorosettes) rather than prominent areas of necrosis.

**Educational objective:**
Glioblastoma multiforme is the most common primary brain tumor in adults. Histopathology showing increased vascularity and pseudopalisading tumor cells around areas of necrosis is diagnostic.

**References**

- 'Pseudopalisading' necrosis in glioblastoma: a familiar morphologic feature that links vascular pathology, hypoxia, and angiogenesis.



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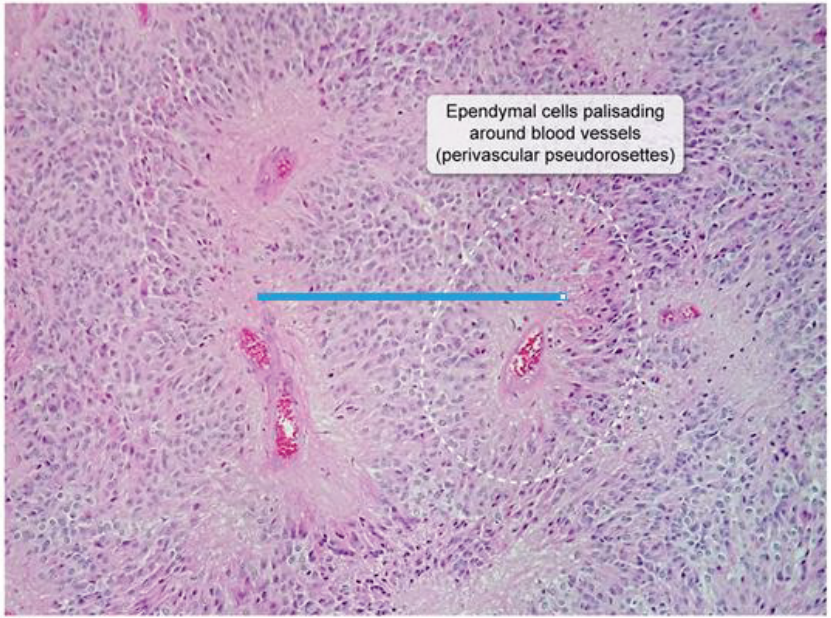
www.ncbi.nlm.nih.gov/pubmed/16783163

xanthoastrocytomas. Although they can rarely progress to GBM, these tumors are usually found in children

Exhibit Display

**Ependymoma**

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A 65-year-old woman was found dead in her house. The family notes that she had difficulty walking over the past few months. The patient had a history of atrial fibrillation treated with anticoagulation therapy. Gross examination shows bruising of the scalp. Autopsy reveals a large epidural hemorrhage with brain herniation; spinal cord evaluation reveals symmetric myelin layer vacuolization and axonal degeneration involving the posterior columns and the lateral corticospinal tracts. Which of the following is the most likely cause of this patient's spinal cord findings?

A. Amyotrophic lateral sclerosis
B. Multiple sclerosis
C. Syringomyelia
D. Tabes dorsalis
E. Thiamine deficiency
F. Varicella-zoster virus infection
G. Vitamin $B_{12}$ deficiency



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A. Amyotrophic lateral sclerosis (10%)
B. Multiple sclerosis (6%)
C. Syringomyelia (4%)
D. Tabes dorsalis (10%)
E. Thiamine deficiency (2%)
F. Varicella-zoster virus infection (0%)
G. Vitamin $B_{12}$ deficiency (66%)

Correct
66%
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10/18/2020


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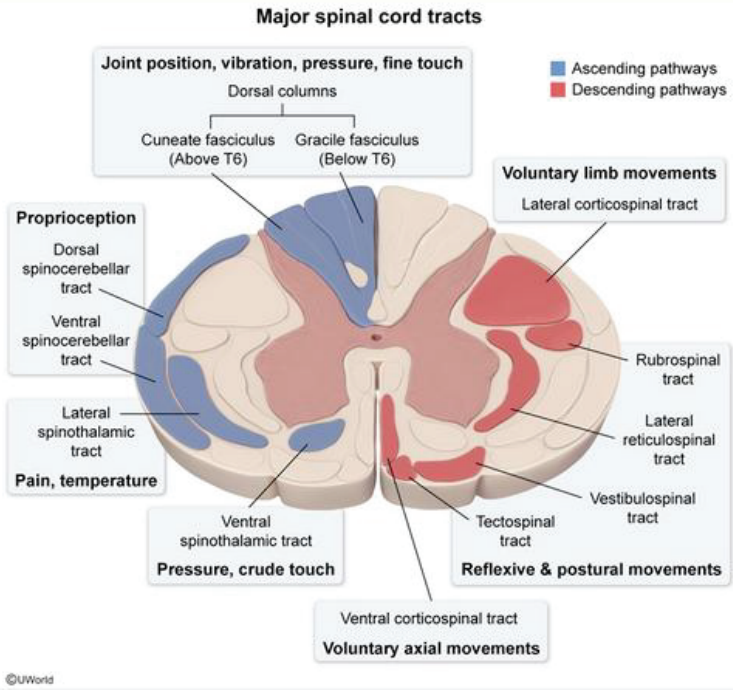


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This patient's history of gait dysfunction and evidence of myelin/axonal degeneration in the dorsal columns and corticospinal tract are highly suggestive of **vitamin $B_{12}$ deficiency**. Vitamin $B_{12}$ is an essential dietary nutrient that contributes to DNA synthesis and repair (via reduction of 5-methyltetrahydrofolate to tetrahydrofolate) and to the generation/maintenance of myelin (via methylation of neuronal lipids and proteins). Although deficiency often presents with **megaloblastic anemia** (due to impaired nuclear maturation of rapidly dividing hematologic cells), many patients develop **neurologic manifestations** due to:

- damage to the dorsal column of the spinal cord, leading to bilateral loss of position and vibration sensation. This commonly results in gait dysfunction, particularly when the patient's eyes are closed (sensory ataxia)
- damage to the lateral corticospinal tracts, leading to upper motor neuron signs (eg, spastic paresis) and positive Babinski sign
- axonal degeneration of the peripheral nerves, leading to numbness, paresthesia, and depressed motor reflexes

The spinal cord damage seen with vitamin $B_{12}$ deficiency is called **subacute combined degeneration**;



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reflexes

The spinal cord damage seen with vitamin $B_{12}$ deficiency is called **subacute combined degeneration**; "combined" refers to the **degeneration** of ascending pathways (**dorsal columns**) and descending pathways (**corticospinal tract**).

**(Choice A)** Amyotrophic lateral sclerosis is marked by progressive upper and lower motor neuron signs. Although damage to the lateral corticospinal tract often occurs, the dorsal columns are generally spared. Most cases present with asymmetric limb weakness, atrophy, and fasciculation due to anterior horn damage.

**(Choice B)** Multiple sclerosis usually causes focal demyelinated plaques within the central nervous system. These are typically asymmetric and in different phases of evolution. This patient's symmetric degeneration of the dorsal columns and corticospinal tract would be unusual.

**(Choice C)** Syringomyelia, a cyst within the spinal cord, can expand over time, leading to central spinal cord injury. The corticospinal tracts and anterior horn are often affected (eg, flaccid paralysis, atrophy). However, syringomyelia would likely be identified on gross autopsy.

**(Choice D)** Tabes dorsalis (a form of neurosyphilis) is associated with damage to the dorsal columns and dorsal nerve roots, leading to loss of position and vibration sensation, sensory gait ataxia, and paresthesia


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However, syringomyelia would likely be identified on gross autopsy.

**(Choice D)** Tabes dorsalis (a form of neurosyphilis) is associated with damage to the dorsal columns and dorsal nerve roots, leading to loss of position and vibration sensation, sensory gait ataxia, and paresthesia of the extremities. However, the lateral corticospinal tracts are not generally affected.

**(Choice E)** Thiamine deficiency causes Wernicke encephalopathy, which often manifests with gait dysfunction, confusion, and oculomotor impairment. However, histopathology generally shows demyelination in the brain (eg, mamillary bodies, thalamus, ocular motor nuclei), not corticospinal tracts and dorsal columns.

**(Choice F)** Varicella-zoster virus infection can cause painful neuritis in the peripheral nervous system. Central nervous system lesions are less common.

**Educational objective:**
Myelopathy associated with vitamin $B_{12}$ deficiency is called subacute combined degeneration. "Combined" refers to myelin degeneration of both the ascending (dorsal columns) and descending (corticospinal tract) pathways. Loss of position and vibration sensation, sensory ataxia, and spastic paresis are common manifestations.



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A 15-year-old boy is brought to the office because of 3 months of sudden, brief jerking movements involving both arms. The episodes usually occur shortly after awakening in the morning and are aggravated by sleep deprivation. The movements are neither suppressible nor preceded by an urge to make a movement. The patient has never lost consciousness and has no known medical conditions. Family history includes a seizure disorder in his uncle. Vital signs are within normal limits. Physical examination shows normal development with no abnormalities. Which of the following is the best initial treatment for this patient?

A. Baclofen
B. Carbamazepine
C. Clonidine
D. Diazepam
E. Propranolol
F. Valproic acid
G. Tetrabenazine



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involving both arms. The episodes usually occur shortly after awakening in the morning and are aggravated by sleep deprivation. The movements are neither suppressible nor preceded by an urge to make a movement. The patient has never lost consciousness and has no known medical conditions. Family history includes a seizure disorder in his uncle. Vital signs are within normal limits. Physical examination shows normal development with no abnormalities. Which of the following is the best initial treatment for this patient?

- A. ~~Baclofen~~ (6%)
- ✗ B. Carbamazepine (23%)
- C. ~~Clonidine~~ (4%)
- D. ~~Diazepam~~ (7%)
- E. ~~Propranolol~~ (5%)
- ✓ F. Valproic acid (47%)
- G. ~~Tetrabenazine~~ (5%)



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| Seizure type | Description | Preferred anticonvulsants |
|---|---|---|
| **Focal onset** (involves a single cerebral hemisphere at onset) | | |
| **Aware** | • No loss of consciousness or postictal state<br>• Motor, sensory, autonomic, or cognitive symptoms | • Carbamazepine*<br>• Lamotrigine<br>• Levetiracetam<br>• Phenytoin* |
| **Impaired awareness** | • Appears awake but consciousness is altered (eg, blank stare)<br>• Postictal state<br>• May have automatisms (eg, lip smacking) | |
| **Generalized onset** (involves both hemispheres at onset) | | |
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |


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| **Generalized onset** (involves both hemispheres at onset) | | |
|---|---|---|
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |
| **Absence** | • Brief episodes of altered consciousness (eg, blank stare)<br>• May have automatisms<br>• Usually no postictal state | • Ethosuxamide<br>• Valproic acid |

*Narrow-spectrum agents can also treat focal-onset seizures that evolve into bilateral tonic-clonic seizures.

This patient most likely has **myoclonic seizures** due to juvenile myoclonic epilepsy (JME), a form of **generalized onset epilepsy** (ie, affecting both cerebral hemispheres at onset) that may be familial. Typically, JME manifests in an otherwise healthy adolescent with myoclonic seizures (ie, **brief, involuntary jerking movements**) involving both upper extremities with preservation of consciousness. Symptoms


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This patient most likely has **myoclonic seizures** due to juvenile myoclonic epilepsy (JME), a form of **generalized onset epilepsy** (ie, affecting both cerebral hemispheres at onset) that may be familial. Typically, JME manifests in an otherwise healthy adolescent with myoclonic seizures (ie, **brief, involuntary jerking movements**) involving both upper extremities with preservation of consciousness. Symptoms usually occur within the first hour of awakening and can be provoked by sleep deprivation. Patients can also develop tonic-clonic and/or absence seizures.

Treatment of generalized onset epilepsies like JME should include a **broad-spectrum anticonvulsant** (eg, **valproic acid**, levetiracetam) which can treat both focal and generalized seizures. In contrast, narrow-spectrum anticonvulsants (eg, carbamazepine, phenytoin) are primarily used only in patients with focal onset seizures and can worsen seizure symptoms in patients with absence or myoclonic seizures **(Choice B)**.

**(Choice A)** Baclofen is a GABA-B agonist that can treat chronic muscle spasticity (eg, cerebral palsy). Patients with chronic muscle spasticity typically have progressive changes in development and muscle tone that would be apparent on physical examination.

**(Choice C)** Clonidine is an alpha-2 adrenergic receptor agonist that may be effective in children with attention-deficit hyperactivity disorder who have failed treatment with stimulants (eg, methylphenidate).



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that would be apparent on physical examination.

**(Choice C)** Clonidine is an alpha-2 adrenergic receptor agonist that may be effective in children with attention-deficit hyperactivity disorder who have failed treatment with stimulants (eg, methylphenidate).

**(Choice D)** Diazepam is a benzodiazepine that can be used acutely to treat prolonged seizures such as status epilepticus (≥5 minutes of continuous seizure activity or >1 seizure without recovery in between). However, diazepam would not be indicated for this patient's brief episodes of myoclonus.

**(Choice E)** Propranolol is a nonselective beta blocker that can treat benign essential tremor, which typically presents in middle-aged adults with bilateral, rhythmic hand tremor that worsens during fine motor activity.

**(Choice G)** Tetrabenazine is a dopamine depletion agent that can treat Tourette syndrome, a disorder characterized by motor and phonic tics that persist for >1 year. Motor tics can manifest as periodic, sudden, jerking movements, but they are usually temporarily suppressible and often preceded by an urge to make the stereotyped movement.

**Educational objective:**
Broad-spectrum anticonvulsants (eg, levetiracetam, valproic acid) treat both focal and generalized onset seizures, whereas narrow-spectrum anticonvulsants (eg, carbamazepine, phenytoin) are primarily used


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**Educational objective:**

Broad-spectrum anticonvulsants (eg, levetiracetam, valproic acid) treat both focal and generalized onset seizures, whereas narrow-spectrum anticonvulsants (eg, carbamazepine, phenytoin) are primarily used only for focal onset seizures. Because the seizures in juvenile myoclonic epilepsy are usually generalized onset (ie, affect both cerebral hemispheres at onset), treatment is with a broad-spectrum agent such as valproic acid.

**References**

- Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data.



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A 64-year-old smoker is evaluated for nagging right shoulder pain that radiates to the ipsilateral arm. The patient also has weakness in the right upper extremity. His symptoms started 2 months ago and have worsened progressively. On neurologic examination, the patient is awake, alert, oriented, and follows commands. He has partial right-sided ptosis with fully intact extraocular movements. His pupils are asymmetric in dim light with 2 mm on the right and 4 mm on the left, but both are reactive to light. The pupils become more symmetric in bright light. The right upper extremity has 3/5 strength and absent deep tendon reflexes. This patient's autonomic dysfunction is most likely a result of a lesion involving which of the following?

A. Autonomic ganglia
B. Brainstem
C. Cerebral cortex
D. Spinal cord
E. Subcortical grey matter
F. Vagus nerve



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worsened progressively. On neurologic examination, the patient is awake, alert, oriented, and follows commands. He has partial right-sided ptosis with fully intact extraocular movements. His pupils are asymmetric in dim light with 2 mm on the right and 4 mm on the left, but both are reactive to light. The pupils become more symmetric in bright light. The right upper extremity has 3/5 strength and absent deep tendon reflexes. This patient's autonomic dysfunction is most likely a result of a lesion involving which of the following?

- A. Autonomic ganglia (51%)
- B. Brainstem (16%)
- C. Cerebral cortex (6%)
- D. Spinal cord (20%)
- E. Subcortical grey matter (3%)
- F. Vagus nerve (2%)

Correct

51%

02 mins, 36 secs

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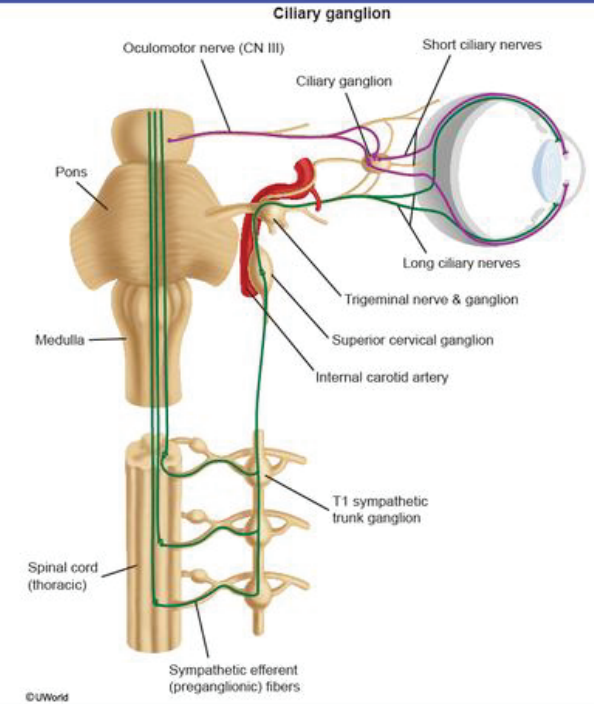


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This patient's smoking history, upper limb pain/weakness, and ipsilateral ptosis and miosis are highly suggestive of a Pancoast tumor. Pancoast tumors are usually non-small cell lung cancers (eg, squamous cell carcinoma, adenocarcinoma) that arise near the superior sulcus (the groove produced by the subclavian artery). Clinical manifestations are determined by the extent of local spread. Compression and invasion of the **brachial plexus** can cause ipsilateral shoulder pain, upper limb paresthesias, and areflexic arm weakness. Involvement of the cervical sympathetic ganglia may lead to Horner's syndrome, which is characterized by ipsilateral:

1. **Partial ptosis** (drooping of upper eyelid), due to denervation of the sympathetically controlled superior tarsal muscle of the upper eyelid.
2. **Miosis** (constricted pupil), due to interruption of the sympathetic fibers to the dilator pupillae muscle, which leads to unopposed parasympathetic influence. Pupil asymmetry is more prominent when examined in dim light due to increased sympathetic activity exacerbating the defect.
3. **Anhidrosis** (impaired sweating), due to loss of sympathetic innervation of the facial sweat glands.

Horner's syndrome can result from disruption at any point along the sympathetic pathway to the eye. First order sympathetic neurons are located in the hypothalamus. Their axons descend through the brainstem to the C8-T2 segments of the spinal cord (ciliospinal center of Budge), where they synapse on second


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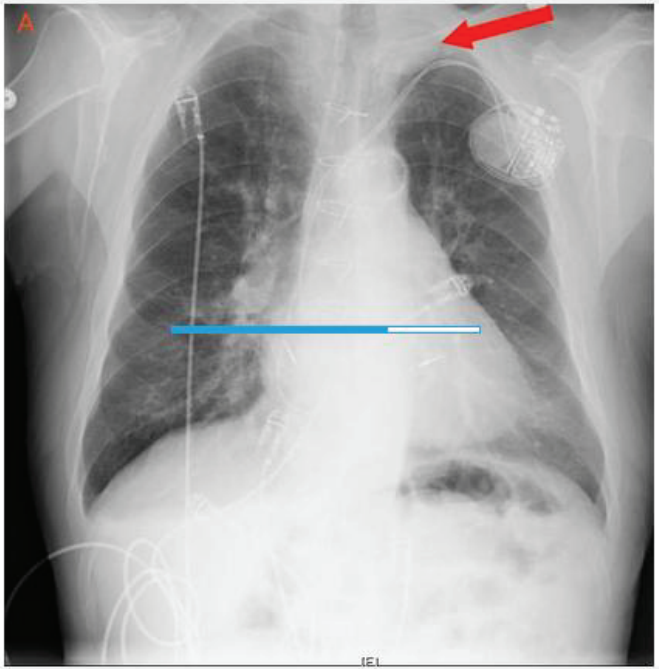
Superior sulcus tumor Superior sulcus tumor

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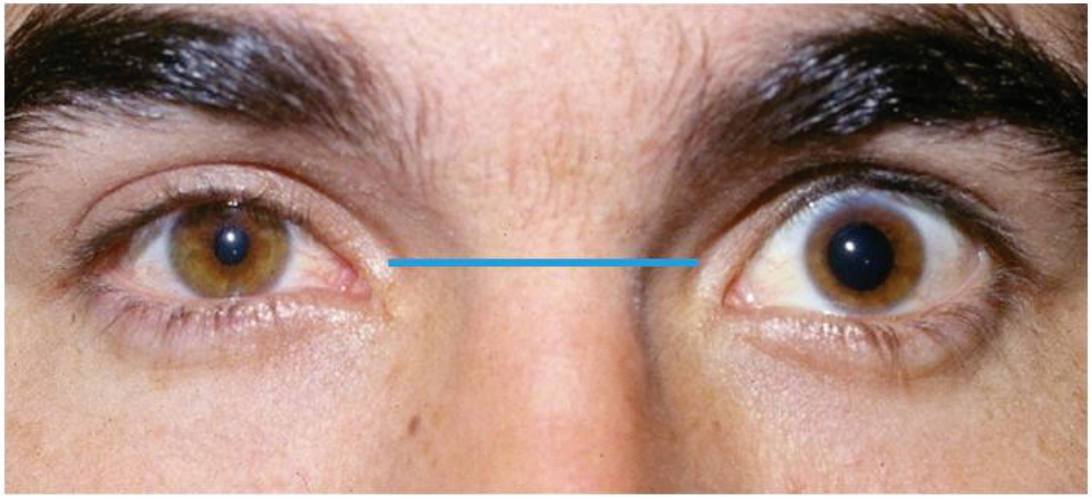

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to the C8-T2 segments of the spinal cord (ciliospinal center of Budge), where they synapse on second order neurons found in the intermediolateral cell column. Second order axons exit the spinal cord through the anterior nerve roots and white communicating rami to reach third order neurons located in the superior cervical ganglion. From here, postganglionic fibers travel along the carotid arteries to reach target tissues in the face and head.

**(Choices B and D)** Both brainstem and spinal cord lesions can cause Horner's syndrome, but this patient's unilateral arm pain and weakness are more suggestive of a lesion affecting the brachial plexus/sympathetic ganglia. Brain stem lesions typically result in crossed signs (eg, contralateral hemiparesis or sensory loss) with cranial nerve abnormalities, diplopia, vertigo, and ataxia. Spinal cord lesions can result in ipsilateral spastic hemiparesis and sensory loss below the level of spinal involvement.

**(Choices C and E)** Damage to the cerebral cortex and basal ganglia is not associated with Horner's syndrome.

**(Choice F)** A vagus nerve (cranial nerve X) lesion may cause ipsilateral paralysis of the soft palate, pharynx, and larynx, producing hoarseness, dysarthria, dysphagia, and loss of the gag reflex (efferent limb). On examination, the uvula will be deviated away from the side of the lesion due to weakness of the levator veli palatini.



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**(Choices C and E)** Damage to the cerebral cortex and basal ganglia is not associated with Horner's syndrome.

**(Choice F)** A vagus nerve (cranial nerve X) lesion may cause ipsilateral paralysis of the soft palate, pharynx, and larynx, producing hoarseness, dysarthria, dysphagia, and loss of the gag reflex (efferent limb). On examination, the uvula will be deviated away from the side of the lesion due to weakness of the levator veli palatini.

**Educational objective:**

Pancoast tumors are non-small cell lung cancers (eg, squamous cell carcinoma, adenocarcinoma) that arise near the superior sulcus. Patients may develop ipsilateral shoulder pain, upper limb paresthesias, and areflexic arm weakness due to involvement of the brachial plexus. Horner's syndrome (eg, ipsilateral partial ptosis, miosis, anhydrosis) can also occur due to involvement of the cervical sympathetic ganglia.

**References**

- Horner syndrome.
- Acquired Horner's syndrome: clinical review.

Anatomy Nervous System Lung cancer



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A 75-year-old man is brought to the emergency department due to problems with vision and right-sided hemisensory loss that started an hour ago. While in the emergency department, his symptoms gradually worsen and he develops a headache. Head CT reveals multiple, small lobar hemorrhages of varying ages in the occipital and parietal areas with a medium-size acute bleed in the left parietooccipital lobe. Two years ago, the patient developed sudden right arm weakness; neuroimaging at that time demonstrated a small left frontal lobe hemorrhage. He has no head trauma and does not use anticoagulants. This patient most likely suffers from which of the following?

A. Arteriovenous malformation
B. Cardiac embolism
C. Carotid artery atherosclerosis
D. Cerebral amyloid angiopathy
E. Charcot-Bouchard aneurysm
F. Hypertensive encephalopathy
G. Hypoxic encephalopathy



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in the occipital and parietal areas with a medium-size acute bleed in the left parietooccipital lobe. Two years ago, the patient developed sudden right arm weakness; neuroimaging at that time demonstrated a small left frontal lobe hemorrhage. He has no head trauma and does not use anticoagulants. This patient most likely suffers from which of the following?

A. Arteriovenous malformation
B. Cardiac embolism
C. Carotid artery atherosclerosis
D. Cerebral amyloid angiopathy
E. Charcot-Bouchard aneurysm
F. Hypertensive encephalopathy
G. Hypoxic encephalopathy
H. Saccular aneurysm

Submit



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A 75-year-old man is brought to the emergency department due to problems with vision and right-sided hemisensory loss that started an hour ago. While in the emergency department, his symptoms gradually worsen and he develops a headache. Head CT reveals multiple, small lobar hemorrhages of varying ages in the occipital and parietal areas with a medium-size acute bleed in the left parietooccipital lobe. Two years ago, the patient developed sudden right arm weakness; neuroimaging at that time demonstrated a small left frontal lobe hemorrhage. He has no head trauma and does not use anticoagulants. This patient most likely suffers from which of the following?

A. ~~Arteriovenous malformation~~ (12%)
B. ~~Cardiac embolism~~ (4%)
C. Carotid artery atherosclerosis (6%)
D. Cerebral amyloid angiopathy (26%)
E. Charcot-Bouchard aneurysm (27%)
F. ~~Hypertensive encephalopathy~~ (14%)
G. ~~Hypoxic encephalopathy~~ (1%)


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This **elderly** patient likely has recurrent lobar hemorrhage due to **cerebral amyloid angiopathy**. Amyloid angiopathy is a consequence of β-amyloid deposition in the walls of small- to medium-sized cerebral arteries, resulting in vessel wall weakening and predisposition to rupture. The disease is not associated with systemic amyloidoses; rather, the amyloidogenic proteins are usually the same as those seen in Alzheimer disease. Amyloid angiopathy is the most common cause of spontaneous **lobar hemorrhage**, particularly in adults age >60. Hemorrhage tends to be recurrent and most often involves the occipital and parietal lobes. Occipital lobe hemorrhage is typically associated with homonymous hemianopsia; parietal hemorrhages can cause contralateral hemisensory loss. Frontal lobe hemorrhage is less common but may result in contralateral hemiparesis.

**(Choice A)** Brain arteriovenous malformation is the most common cause of intracranial hemorrhage in children and tends to be a single lesion. This patient's older age and multifocal hemorrhages make the diagnosis less likely.

**(Choices B and C)** Carotid artery atherosclerosis and cardiac embolism may cause acute ischemic stroke, which typically presents with sudden neurologic deficits that are maximal at symptom onset. Embolic stroke can present with multiple infarcts involving the cerebral cortex and has a higher likelihood of spontaneous hemorrhagic transformation. However, hemorrhagic transformation would be rare within


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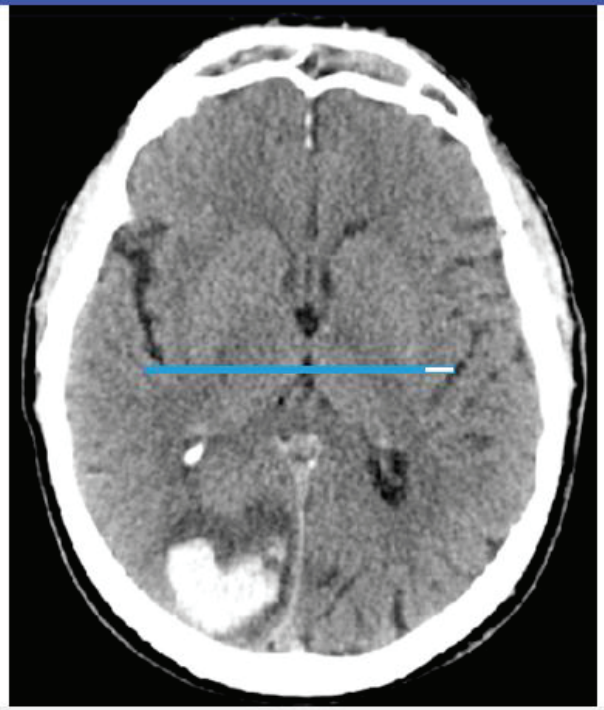

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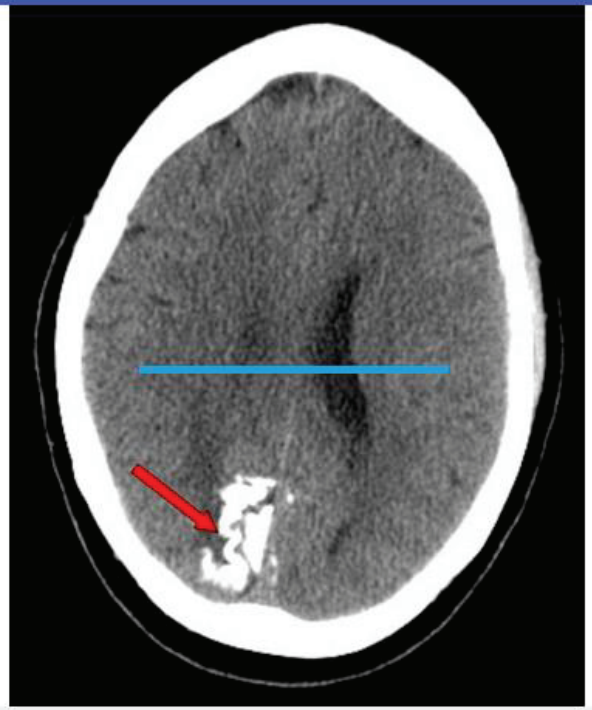

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spontaneous hemorrhagic transformation. However, hemorrhagic transformation would be rare within hours of symptom onset. In addition, this patient's gradually worsening symptoms are more consistent with hemorrhagic stroke.

**(Choice E)** Charcot-Bouchard aneurysm rupture is usually due to chronic hypertension and typically causes hemorrhage involving deep brain structures (eg, basal ganglia, cerebellar nuclei, thalamus, pons). This patient's recurrent lobar hemorrhages make this less likely.

**(Choice F)** Hypertensive encephalopathy is characterized by **progressive** headache and nausea/vomiting followed by nonlocalizing neurologic symptoms (eg, confusion). This patient's focal neurologic deficits and evidence of hemorrhage on neuroimaging exclude this diagnosis.

**(Choice G)** Hypoxic encephalopathy occurs from global interruption of the cerebral blood supply (eg, due to cardiac arrest). It most often presents with decreased consciousness (eg, coma, vegetative state) as opposed to focal neurologic deficits with lobar hemorrhage.

**(Choice H)** Saccular aneurysm rupture is typically associated with subarachnoid hemorrhage as opposed to intraparenchymal hematoma. Patients usually have an abrupt onset of severe headache (thunderclap headache), and focal neurologic deficits are less common. On CT, subarachnoid hemorrhage appears as hyperattenuation of the sulci and basal cisterns.


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spontaneous hemorrhagic transformation. However, hemorrhagic transformation would be rare within

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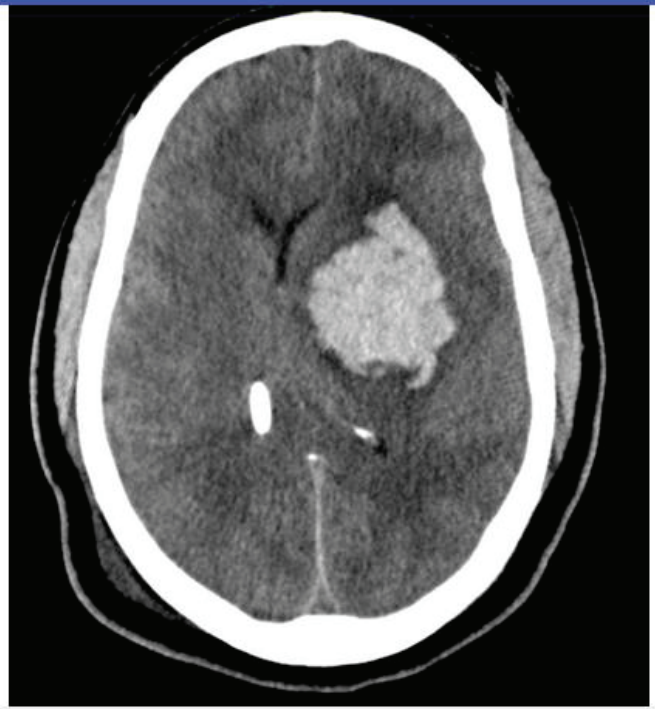

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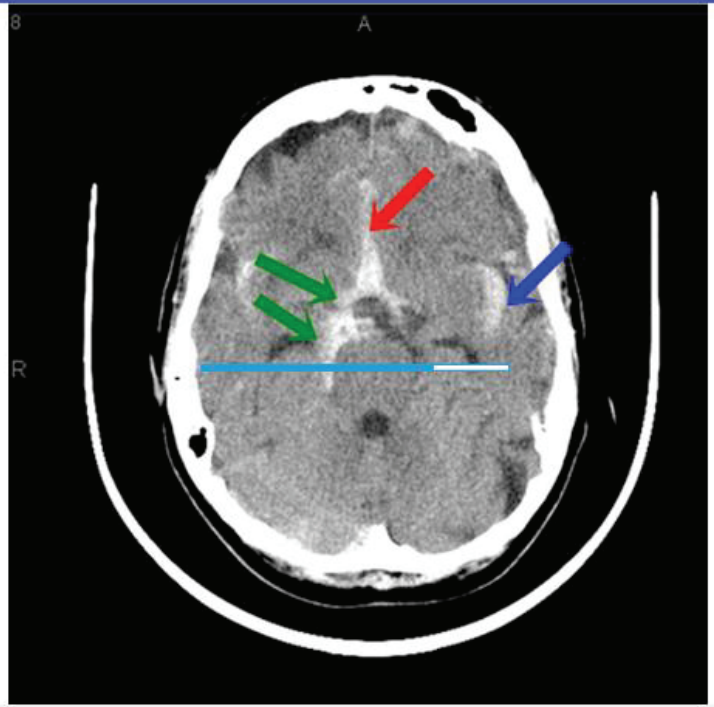


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evidence of hemorrhage on neuroimaging exclude this diagnosis.

**(Choice G)** Hypoxic encephalopathy occurs from global interruption of the cerebral blood supply (eg, due to cardiac arrest). It most often presents with decreased consciousness (eg, coma, vegetative state) as opposed to focal neurologic deficits with lobar hemorrhage.

**(Choice H)** Saccular aneurysm rupture is typically associated with subarachnoid hemorrhage as opposed to intraparenchymal hematoma. Patients usually have an abrupt onset of severe headache (thunderclap headache), and focal neurologic deficits are less common. On CT, subarachnoid hemorrhage appears as hyperattenuation of the sulci and basal cisterns.

**Educational objective:**

Cerebral amyloid angiopathy is the most common cause of spontaneous lobar hemorrhage, particularly in the elderly. The most common sites of hemorrhage include the occipital and parietal lobes.

**References**

- Cerebral amyloid angiopathy-related hemorrhages.

| Pathology | Nervous System | Hemorrhagic stroke |
|---|---|---|
| Subject | System | Topic |



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A 58-year-old homeless man is brought to the emergency department after being found unresponsive on a sidewalk. The patient has been hospitalized on several occasions for alcohol and illicit drug intoxication. He also has a history of hypertension but is not adherent with medical therapy. On arrival, the patient is obtunded, febrile, and hypotensive. Physical examination reveals lung crackles and a new blowing diastolic murmur consistent with aortic regurgitation. Appropriate treatment is started, but the patient dies several days later. Autopsy examination shows symmetric, bilateral wedge-shaped strips of necrosis over the cerebral convexity, parallel and a few centimeters lateral to the interhemispheric cerebral fissure.

Which of the following is the most likely cause of this patient's cerebral findings?

A. Amyloid deposition in cerebral arteries
B. Cerebral embolization of heart valve vegetations
C. Generalized reduction of cerebral perfusion
D. Hypertension-induced microaneurysm formation
E. Localized weakness and rupture of arterial walls



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sidewalk. The patient has been hospitalized on several occasions for alcohol and illicit drug intoxication. He also has a history of hypertension but is not adherent with medical therapy. On arrival, the patient is obtunded, febrile, and hypotensive. Physical examination reveals lung crackles and a new blowing diastolic murmur consistent with aortic regurgitation. Appropriate treatment is started, but the patient dies several days later. Autopsy examination shows symmetric, bilateral wedge-shaped strips of necrosis over the cerebral convexity, parallel and a few centimeters lateral to the interhemispheric cerebral fissure. Which of the following is the most likely cause of this patient's cerebral findings?

A. Amyloid deposition in cerebral arteries (2%)
B. Cerebral embolization of heart valve vegetations (37%)
C. Generalized reduction of cerebral perfusion (45%)
D. Hypertension-induced microaneurysm formation (10%)
E. Localized weakness and rupture of arterial walls (3%)

Correct
45%
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03/21/2021


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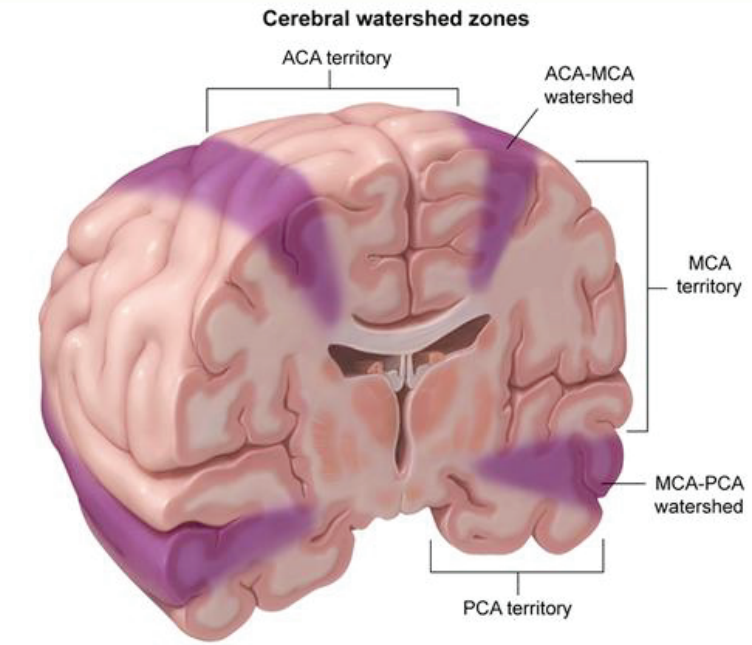


**ACA** = anterior cerebral artery; **MCA** = middle cerebral artery; **PCA** = posterior cerebral artery.
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**ACA** = anterior cerebral artery; **MCA** = middle cerebral artery; **PCA** = posterior cerebral artery.

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This patient with a history of drug use developed fever and new-onset aortic regurgitation, which are suggestive of endocarditis. His pulmonary edema (crackles) and hypotension are due to subsequent **cardiogenic shock**. On autopsy, the symmetric, bilateral wedge-shaped strips of necrosis over the cerebral convexity are characteristic of **global cerebral ischemia**.

Profound **systemic hypotension** (eg, cardiogenic shock, cardiopulmonary arrest) diminishes blood supply to the entire brain, resulting in **neuron cell death** in areas that are vulnerable to hypoxia. This includes brain regions with high metabolic demand (eg, hippocampus, cerebellar Purkinje cells) and areas supplied by the distal-most branches of cerebral arteries (**watershed zones**). These border zones are located between areas supplied by the anterior, middle, and posterior cerebral arteries and are vulnerable because of low baseline perfusion pressure. The resulting necrosis occurs in bilateral, **wedge-shaped** strips that can extend from the frontal to occipital lobe and are located parallel and a few centimeters lateral to the interhemispheric fissure.

**(Choice A)** Cerebral amyloid angiopathy typically affects patients over the age of 70 and results in lobar hemorrhages (eg, occipital, parietal) rather than ischemia. Amyloidosis can also cause cardiomyopathy, although patients typically develop right-sided heart failure (eg, edema, ascites) rather than valvular



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although patients typically develop right-sided heart failure (eg, edema, ascites) rather than valvular insufficiency.

**(Choice B)** Although infectious endocarditis frequently causes embolization of bacterial vegetations, cardiac embolism would likely cause multiple scattered infarcts in an **asymmetric** pattern within different major vascular territories (eg, middle and anterior cerebral artery). This patient's symmetric, bilateral infarcts correspond to the cortical watershed regions and are more suggestive of global cerebral ischemia.

**(Choice D)** Charcot-Bouchard aneurysms form as a result of chronic hypertension, and a rupture causes intracerebral hemorrhage typically involving deep brain structures (eg, basal ganglia, cerebellar nuclei, thalamus, pons).

**(Choice E)** Saccular aneurysms, which occur at areas of weakness in cerebral arteries, typically cause subarachnoid hemorrhage after a rupture rather than cerebral ischemia. Patients usually have sudden-onset severe (thunderclap) headache and meningismus.

**Educational objective:**
Sustained cerebral hypoperfusion (eg, hypotension, shock) may cause global cerebral ischemia and watershed infarction. These watershed zones are located at the borders between areas perfused by the anterior, middle, and posterior cerebral arteries and typically appear as symmetric, bilateral wedge-shaped


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although patients typically develop right-sided heart failure (eg, edema, ascites) rather than valvular

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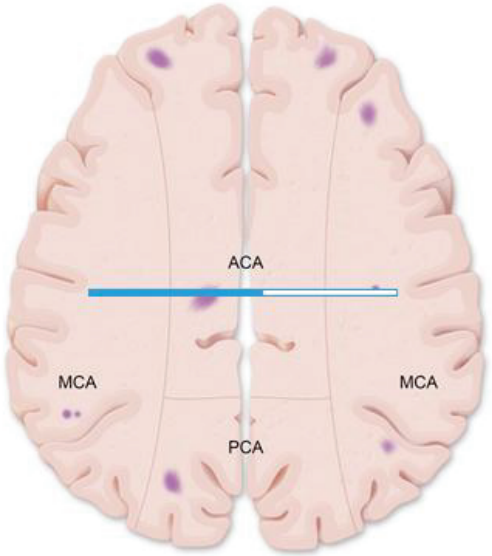
Cortical embolic infarcts




**ACA** = anterior cerebral artery; **MCA** = middle cerebral artery; **PCA** = posterior cerebral artery.

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although patients typically develop right-sided heart failure (eg, edema, ascites) rather than valvular

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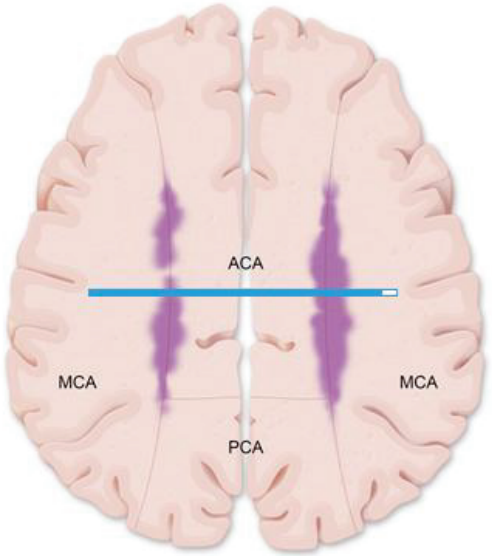
Cortical watershed infarcts




**ACA** = anterior cerebral artery; **MCA** = middle cerebral artery; **PCA** = posterior cerebral artery.

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major vascular territories (eg, middle and anterior cerebral artery). This patient's symmetric, bilateral infarcts correspond to the cortical watershed regions and are more suggestive of global cerebral ischemia.

**(Choice D)** Charcot-Bouchard aneurysms form as a result of chronic hypertension, and a rupture causes intracerebral hemorrhage typically involving deep brain structures (eg, basal ganglia, cerebellar nuclei, thalamus, pons).

**(Choice E)** Saccular aneurysms, which occur at areas of weakness in cerebral arteries, typically cause subarachnoid hemorrhage after a rupture rather than cerebral ischemia. Patients usually have sudden-onset severe (thunderclap) headache and meningismus.

**Educational objective:**

Sustained cerebral hypoperfusion (eg, hypotension, shock) may cause global cerebral ischemia and watershed infarction. These watershed zones are located at the borders between areas perfused by the anterior, middle, and posterior cerebral arteries and typically appear as symmetric, bilateral wedge-shaped strips of necrosis over the cerebral convexity, parallel and adjacent to the interhemispheric fissure.

**References**

- Border zone infarcts: pathophysiologic and imaging characteristics



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A 12-year-old boy is brought to the office by his mother due to headaches and gait instability. His symptoms began several months ago and have progressively worsened. MRI of the brain is shown in the image below.

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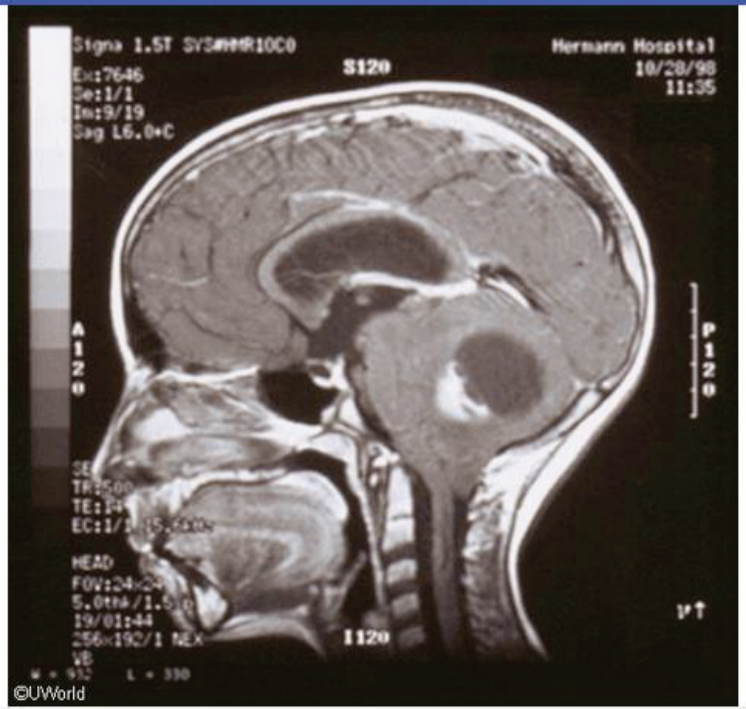


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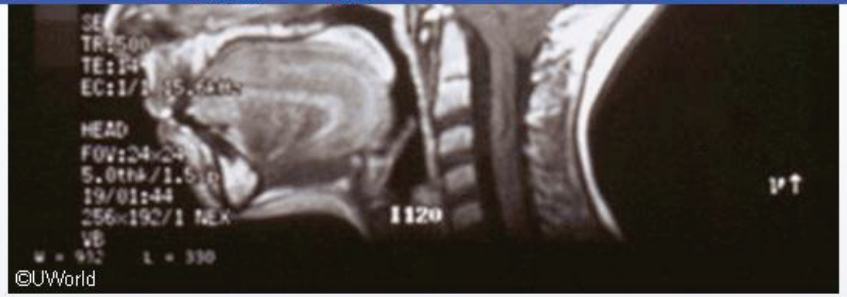


Which of the following is the most likely diagnosis?

A. Ependymoma

B. Glioblastoma multiforme

C. Medulloblastoma

D. Oligodendroglioma

E. Pilocytic astrocytoma

Submit



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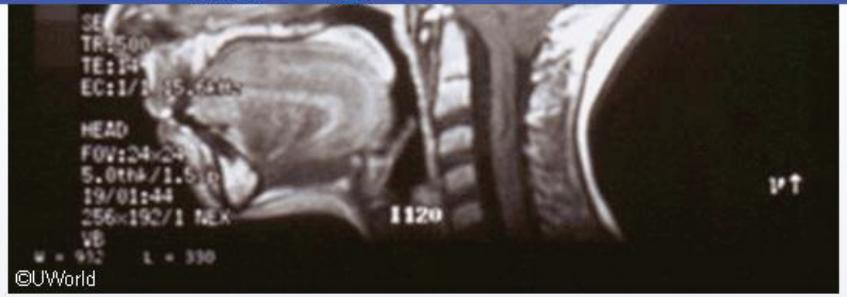


Which of the following is the most likely diagnosis?

A. ~~Ependymoma~~ (9%)

B. ~~Glioblastoma multiforme~~ (4%)

C. Medulloblastoma (38%)

D. ~~Oligodendroglioma~~ (1%)

✓ E. Pilocytic astrocytoma (46%)

Correct

46%

01 min, 29 secs

11/30/2020



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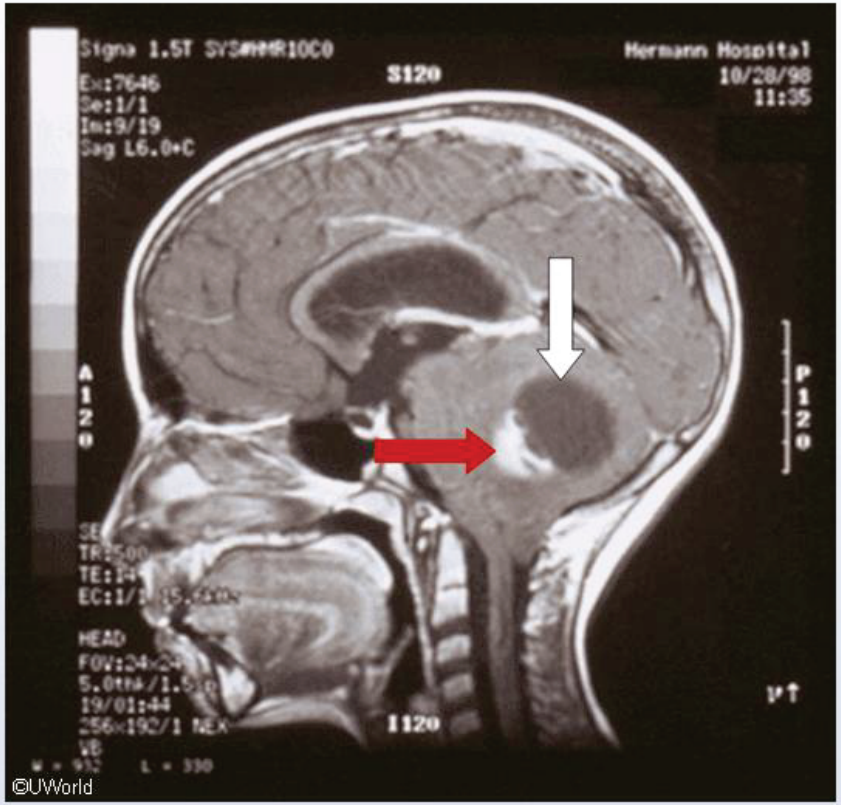

Brain tumors are the second most common childhood cancer (after leukemia) and the most common solid organ tumors of childhood. This child with a heterogeneous, well-circumscribed cerebellar mass most likely has a **pilocytic astrocytoma**, the most common type of brain tumor in children.

Pilocytic astrocytomas are **low-grade** gliomas that occur most frequently in the **cerebellum**. Patients typically have headaches and cerebellar findings (eg, loss of balance, incoordination). Imaging (shown above) reveals a well-demarcated lesion comprised of **cystic and solid components** (white and red arrows, respectively). Microscopic examination shows pilocytic astrocytes with bundles of **glial fibrillary acidic protein (GFAP)-positive** hairlike processes and classic **Rosenthal fibers** (eosinophilic intracytoplasmic inclusions). Due to the slow-growing (benign) nature, the majority of patients can be treated with surgical resection and have a favorable prognosis.

**(Choice A)** Ependymomas are rare tumors arising from the ependymal lining of the ventricle. They commonly occupy the 4th ventricle and can cause hydrocephalus by obstructing the flow of cerebrospinal fluid. Perivascular pseudorosettes are present on microscopy.

**(Choice B)** Glioblastoma multiforme, a tumor arising from GFAP-positive astrocytes, occurs most frequently in adults and is typically located within the cerebral hemispheres (often crossing the corpus callosum). Pseudopalisading pleomorphic cells with areas of necrosis are seen on microscopy.



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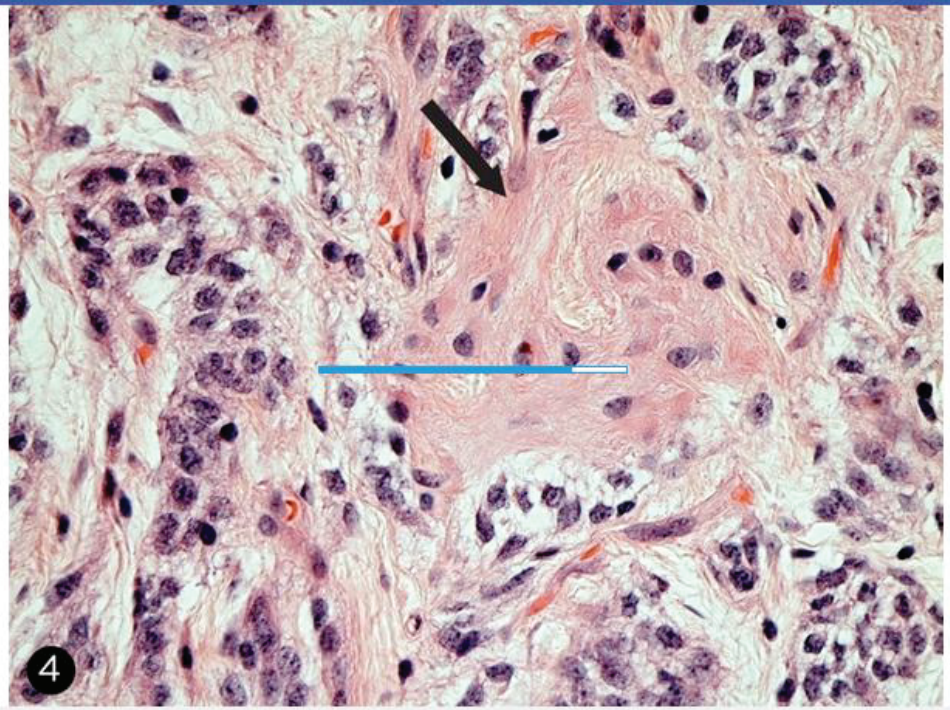


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callosum). Pseudopalisading pleomorphic cells with areas of necrosis are seen on microscopy.



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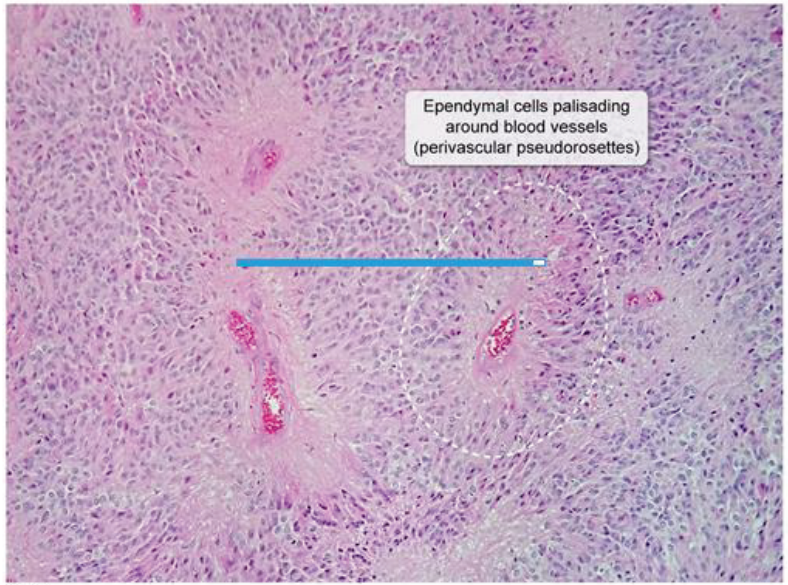
Ependymoma Ependymoma

**Ependymoma**

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callosum). Pseudopalisading pleomorphic cells with areas of necrosis are seen on microscopy.



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**(Choice B)** Glioblastoma multiforme, a tumor arising from GFAP-positive astrocytes, occurs most frequently in adults and is typically located within the cerebral hemispheres (often crossing the corpus callosum). Pseudopalisading pleomorphic cells with areas of necrosis are seen on microscopy.

**(Choice C)** Medulloblastoma is the most common *malignant* childhood brain cancer. It is located exclusively in the cerebellum; however, it is not cystic like pilocytic astrocytoma. Imaging reveals a solid lesion (encircled) that can compress the 4th ventricle, causing hydrocephalus (arrow). It is composed of small cells with hyperchromatic nuclei that form Homer Wright rosettes (groupings of cells surrounding the neuropil).

**(Choice D)** Oligodendrogliomas, rare in children, are frequently calcified, well-circumscribed masses located in the frontal lobe. Microscopy shows uniform cells with a "fried egg" appearance (ie, round nuclei with clear cytoplasm) surrounded by anastomosing capillaries arranged in a "chicken-wire" pattern.

**Educational objective:**

Pilocytic astrocytomas are the most common brain tumors in children. They frequently arise in the cerebellum and can be differentiated from medulloblastomas by the presence of both cystic and solid components on imaging.

**References**


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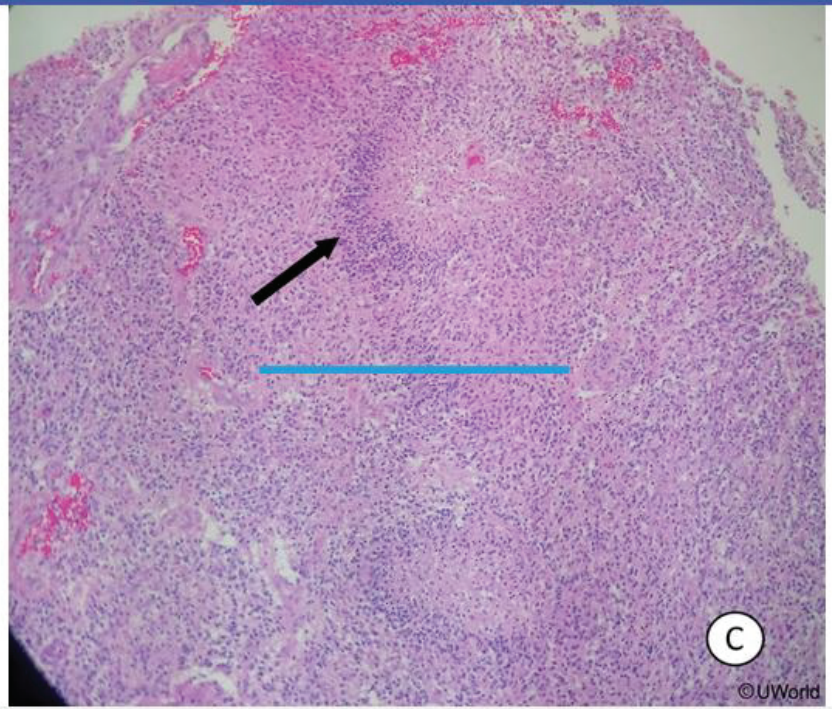


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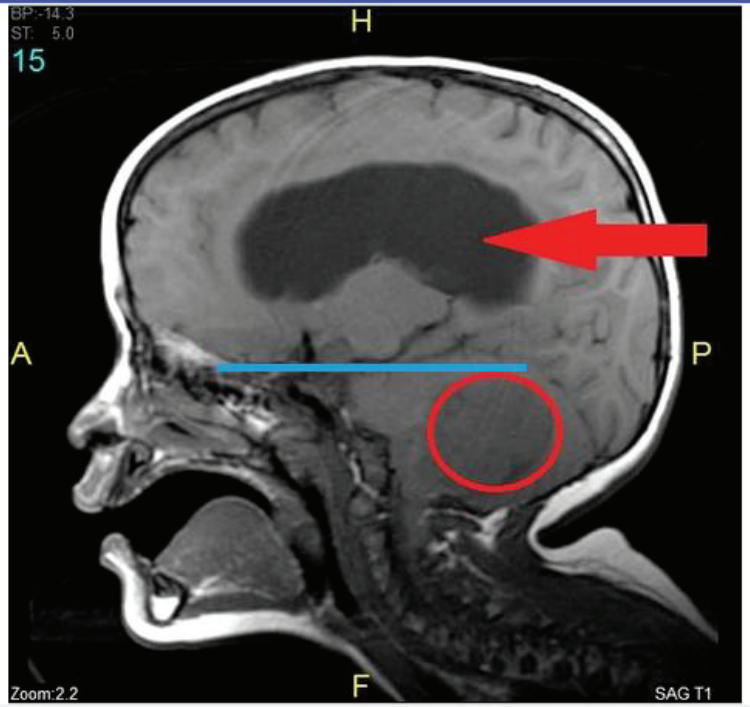


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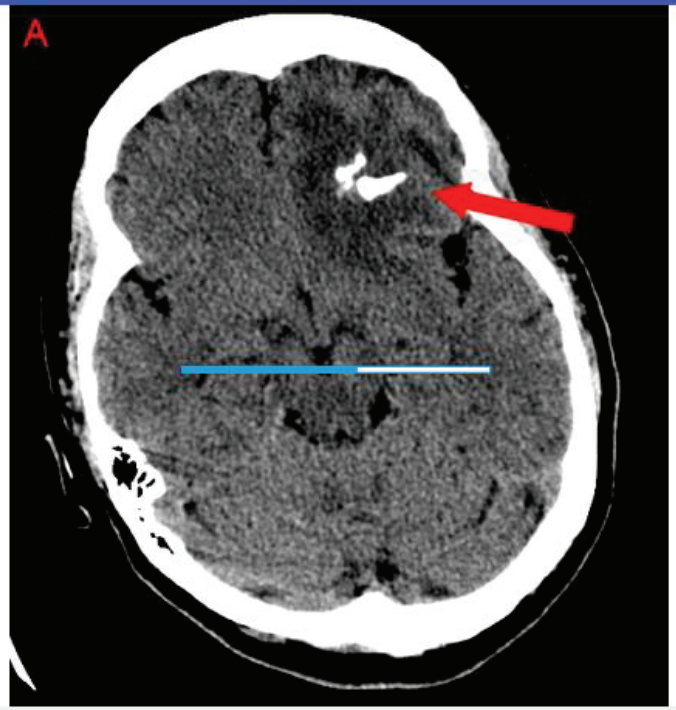


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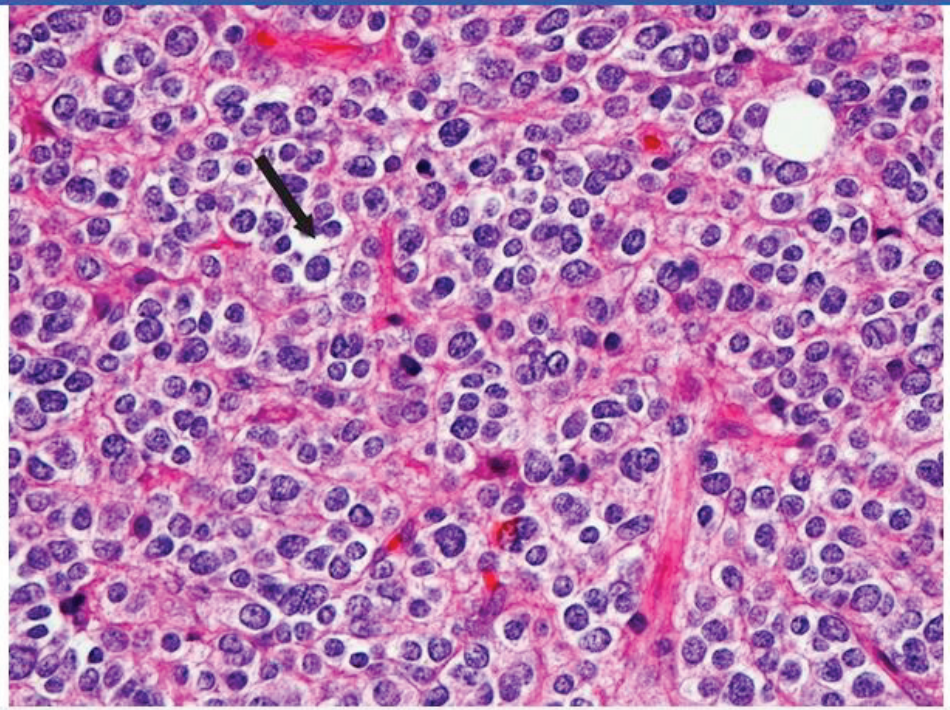

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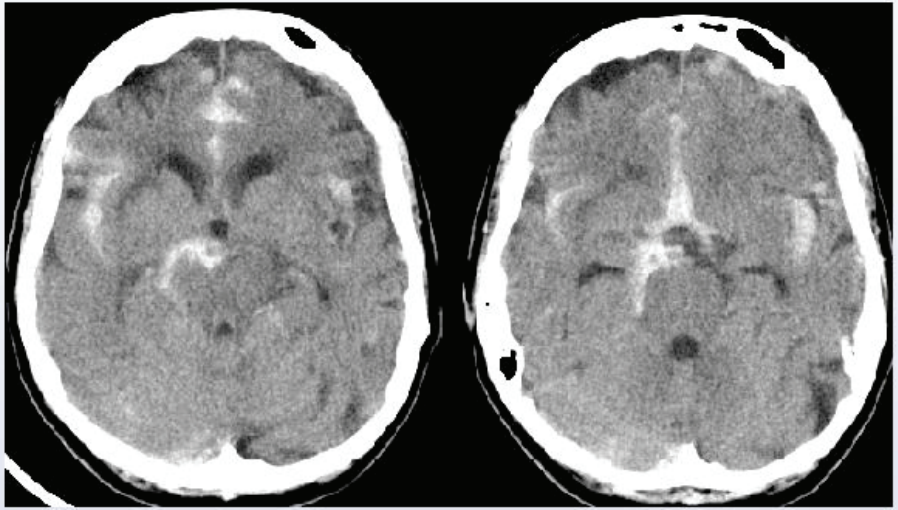
A 43-year-old woman is brought to the emergency department because of a sudden and severe headache. Her blood pressure is 160/90 mm Hg and pulse is 90/min. Her pupils are symmetric and reactive to light and she can move all four extremities without weakness. CT of her head is shown below.



This patient's condition is most likely caused by which of the following?

A. Carotid artery atherosclerosis



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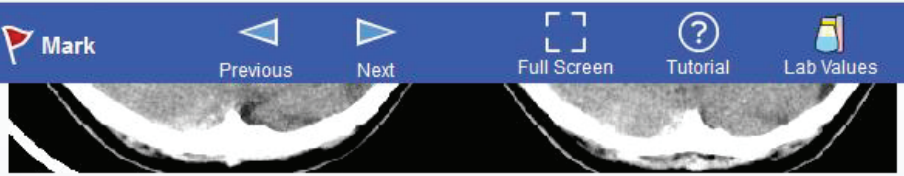

This patient's condition is most likely caused by which of the following?

A. Carotid artery atherosclerosis
B. Cardiac embolism
C. Hypoxic encephalopathy
D. Hypertensive encephalopathy
E. Large vessel arteritis
F. Hypertensive arteriolar sclerosis
G. Cerebral amyloid angiopathy
H. Rupture of saccular aneurysm
I. Charcot-Bouchard aneurysm


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This patient's condition is most likely caused by which of the following?

- A. Carotid artery atherosclerosis (1%)
- B. Cardiac embolism (0%)
- C. Hypoxic encephalopathy (1%)
- D. Hypertensive encephalopathy (10%)
- E. Large vessel arteritis (2%)
- F. Hypertensive arteriolar sclerosis (5%)
- G. Cerebral amyloid angiopathy (2%)
- H. Rupture of saccular aneurysm (62%) ✓
- I. Charcot-Bouchard aneurysm (13%)

Correct

62%

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10/09/2020



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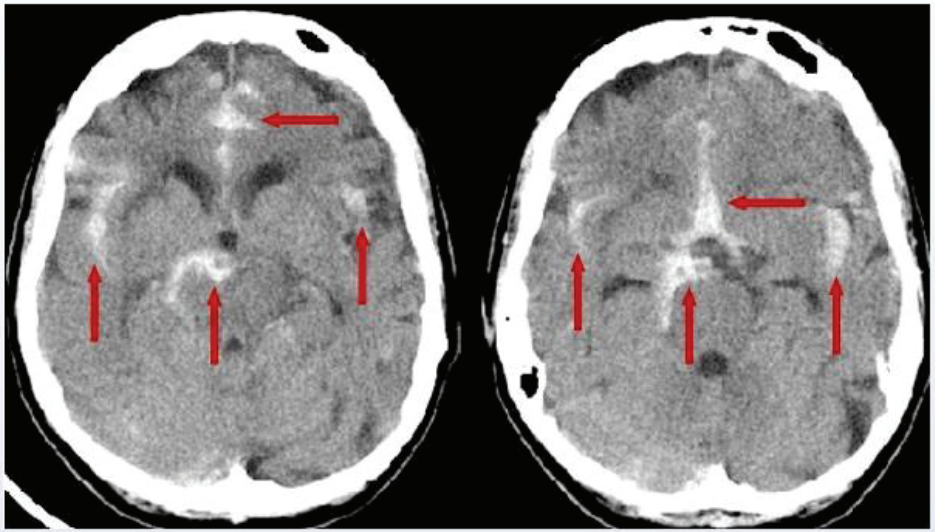

Clinically, the abrupt onset of a severe headache is very characteristic of subarachnoid hemorrhage (SAH), and the above non-contrast CT scan confirms this diagnosis (note the hyperdensity seen within the cisterns/sulci, arrows). The generalized, severe headache of SAH is often described by patients as "the worst headache of my life." Fever and nuchal rigidity may also be present. Focal neurological deficits are usually not present.

Saccular (berry) aneurysms are the most common cause of SAH. These aneurysms usually occur at the


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Saccular (berry) aneurysms are the most common cause of SAH. These aneurysms usually occur at the circle of Willis, with the anterior communicating artery being the most common site. Berry aneurysms are associated with Ehlers-Danlos syndrome and autosomal dominant polycystic kidney disease. Arteriovenous malformations also predispose certain individuals to SAH.

In SAH, blood accumulates between the arachnoid and pia mater. A CT scan without contrast is diagnostic. Lumbar puncture reveals gross blood or xanthochromia (yellow discoloration of cerebrospinal fluid).

**(Choice G)** Cerebral amyloid angiopathy occurs in elderly patients. It may be asymptomatic or may lead to recurrent intracerebral hemorrhage. These bleeds usually affect small areas of the cerebral hemispheres and present with headache and focal neurologic deficits (i.e., paresis, sensory loss, etc).

**(Choice I)** Charcot-Bouchard aneurysms are small in size (< 1 mm in diameter) and occur in patients with long-standing hypertension. They are found in the arterioles that supply the basal ganglia, internal capsule, and deep white matter. Charcot-Bouchard aneurysms can rupture and cause intracerebral hemorrhage, not SAH.

**Educational objective:**

Subarachnoid hemorrhage presents with a generalized, excruciating headache. It is classically described


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**(Choice G)** Cerebral amyloid angiopathy occurs in elderly patients. It may be asymptomatic or may lead to recurrent intracerebral hemorrhage. These bleeds usually affect small areas of the cerebral hemispheres and present with headache and focal neurologic deficits (i.e., paresis, sensory loss, etc).

**(Choice I)** Charcot-Bouchard aneurysms are small in size (< 1 mm in diameter) and occur in patients with long-standing hypertension. They are found in the arterioles that supply the basal ganglia, internal capsule, and deep white matter. Charcot-Bouchard aneurysms can rupture and cause intracerebral hemorrhage, not SAH.

**Educational objective:**

Subarachnoid hemorrhage presents with a generalized, excruciating headache. It is classically described by patients as "the worst headache of my life." Subarachnoid hemorrhage usually occurs due to rupture of saccular (berry) aneurysms or arteriovenous malformations. Berry aneurysms of the circle of Willis are associated with autosomal dominant polycystic kidney disease.

| Pathology | Nervous System | Subarachnoid hemorrhage |
|---|---|---|
| Subject | System | Topic |

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A 15-year-old boy is evaluated for progressive lower extremity weakness. The patient has had difficulty running and keeping up with peers for the past several years and has sprained his ankles on multiple occasions. His father also experienced similar symptoms beginning at the same age and became wheelchair bound. Physical examination shows weakness and atrophy of the distal lower extremity muscles. There is bilateral pes cavus deformity. Ankle reflexes are absent, and sensation to vibration is also absent in the feet. Abnormal function of which of the following is the most likely cause of this patient's condition?

A. Muscle dystrophin
B. Myelin protein
C. Ryanodine receptors
D. Synaptic vesicles
E. Tau protein

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A 15-year-old boy is evaluated for progressive lower extremity weakness. The patient has had difficulty running and keeping up with peers for the past several years and has sprained his ankles on multiple occasions. His father also experienced similar symptoms beginning at the same age and became wheelchair bound. Physical examination shows weakness and atrophy of the distal lower extremity muscles. There is bilateral pes cavus deformity. Ankle reflexes are absent, and sensation to vibration is also absent in the feet. Abnormal function of which of the following is the most likely cause of this patient's condition?

A. ~~Muscle dystrophin~~ (36%)
B. Myelin protein (54%)
C. ~~Ryanodine receptors~~ (3%)
D. ~~Synaptic vesicles~~ (4%)
E. Tau protein (2%)

54%
01 min, 58 secs
12/16/2020



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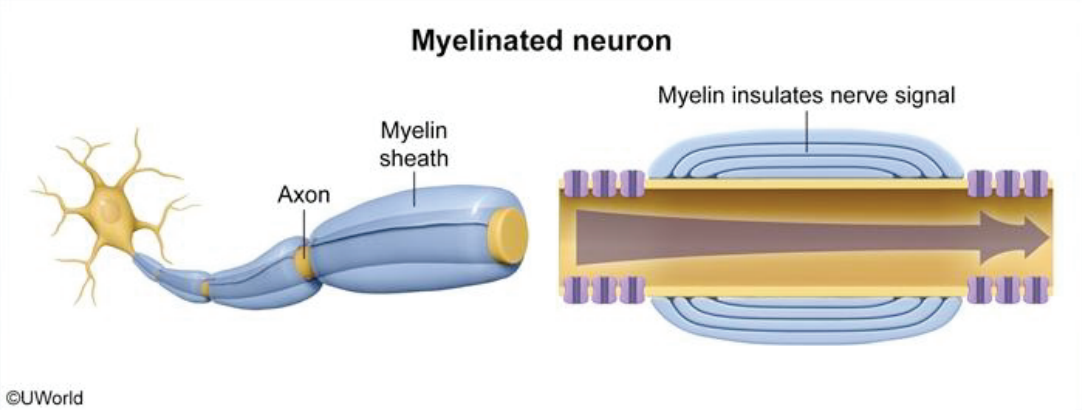


This adolescent with lower extremity weakness, muscle atrophy, and peripheral neuropathy (ie, decreased vibratory sense, absent ankle reflex) likely has **Charcot-Marie-Tooth disease (CMT)**. CMT is a group of **hereditary peripheral neuropathies** characterized by mutations in genes coding for peripheral nerve axonal or **myelin proteins**. The most common subtype, CMT1, occurs due to an autosomal dominant mutation in the *PMP22* gene.

Manifestations of CMT depend on the underlying genetic abnormality; however, most cases present in **adolescence** or early adulthood with progressive, symmetric **distal muscle atrophy** and **weakness**.


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Manifestations of CMT depend on the underlying genetic abnormality; however, most cases present in **adolescence** or early adulthood with progressive, symmetric **distal muscle atrophy** and **weakness**. Initial manifestations often include frequent **ankle sprains** or difficulty with exercise. Physical examination typically demonstrates muscle wasting most prominent in the distal lower extremities, with **sensory loss, areflexia, pes cavus** (ie, high arches), and hammer toes. Upper extremity involvement (ie, intrinsic musculature of the hands) typically occurs later in the disease course.

**(Choice A)** Duchenne and Becker muscular dystrophy are X-linked inherited disorders caused by abnormalities in muscle dystrophin. Patients also develop distal limb weakness but present with a waddling gait and pseudohypertrophy (rather than atrophy) of the calf muscles.

**(Choice C)** Malignant hyperthermia occurs in patients with abnormal ryanodine receptors, which allow excessive calcium accumulation within the skeletal muscle when exposed to volatile anesthetics (eg, halothane, isoflurane). This results in sustained muscle contraction, leading to muscle rigidity, hyperthermia, hypercarbia, and rhabdomyolysis.

**(Choice D)** Botulinum toxin cleaves SNARE proteins within neurons, preventing the synaptic vesicle from fusing to the cell membrane and releasing neurotransmitters. Botulism typically causes acute-onset cranial neuropathies (eg, dysarthria, ptosis) and descending muscle weakness after toxin ingestion (eg, eating


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**(Choice D)** Botulinum toxin cleaves SNARE proteins within neurons, preventing the synaptic vesicle from fusing to the cell membrane and releasing neurotransmitters. Botulism typically causes acute-onset cranial neuropathies (eg, dysarthria, ptosis) and descending muscle weakness after toxin ingestion (eg, eating contaminated home-canned food) or spore exposure (eg, giving honey to an infant). Muscle wasting is unexpected.

**(Choice E)** Hyperphosphorylated tau protein is seen in multiple neurodegenerative diseases (eg, Alzheimer dementia, frontotemporal dementia). These typically occur in elderly patients and present with progressive impairments in cognitive function, not muscle atrophy.

**Educational objective:**

Charcot-Marie-Tooth is a group of hereditary peripheral neuropathies characterized by mutations in genes coding for peripheral nerve axonal or myelin proteins. Manifestations typically include progressive, symmetric distal muscle atrophy and weakness most prominent in the feet and calf musculature, with sensory loss, areflexia, pes cavus (ie, high arches), and hammer toes.

| Pathology | Nervous System | Charcot marie tooth disease |
|---|---|---|
| Subject | System | Topic |

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A 65-year-old man with a long history of smoking comes to the office due to a nonproductive cough over the last several months. He recently developed left shoulder pain, persistent hiccups, and dyspnea. His temperature is 36.7 C (98 F), blood pressure is 140/85 mm Hg, and pulse is 76/min. Physical examination reveals decreased breath sounds on the left side. Chest x-ray shows a large left lung mass. Compression of a nerve arising from which of the following locations is most likely causing this patient's recent symptoms?

- A. Brainstem
- B. C1-C3
- C. C3-C5
- D. C5-C8
- E. T1-T2

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A 65-year-old man with a long history of smoking comes to the office due to a nonproductive cough over the last several months. He recently developed left shoulder pain, persistent hiccups, and dyspnea. His temperature is 36.7 C (98 F), blood pressure is 140/85 mm Hg, and pulse is 76/min. Physical examination reveals decreased breath sounds on the left side. Chest x-ray shows a large left lung mass. Compression of a nerve arising from which of the following locations is most likely causing this patient's recent symptoms?

- A. Brainstem (4%)
- B. C1-C3 (3%)
- ✓ C. C3-C5 (76%)
- D. C5-C8 (10%)
- E. T1-T2 (4%)

Correct

76% Answered correctly

01 min, 20 secs Time Spent

10/02/2020 Last Updated



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**Lung cancers** are prone to early local and distant spread. Intrathoracic expansion of a tumor can cause a number of distinctive syndromes, including **phrenic nerve** irritation and palsy.

The phrenic nerve arises from the **C3-C5** cervical segments and descends through the neck and thorax to innervate the ipsilateral hemidiaphragm. Phrenic nerve **irritation** can cause dyspnea, hiccups (diaphragmatic irritation), and **referred pain to the shoulder** (area innervated by supraclavicular nerve originating from C3 and C4). Phrenic nerve **palsy** is associated with respiratory distress and diminished breath sounds on the affected side, with elevation of the affected hemidiaphragm on chest x-ray. Upward movement of the affected hemidiaphragm with inspiration is seen on fluoroscopy.

Other syndromes that may occur due to local spread of a lung tumor include:

- **Horner syndrome** (ipsilateral miosis, ptosis, and anhydrosis) occurs in association with tumors of the lung apex (**Pancoast tumor**) that disrupt the oculosympathetic nerve pathway. Lung cancer in this location can also invade the rami of the **brachial plexus** (C5-T1) and cause shoulder pain **(Choices D and E).**
- A centrally located tumor or mediastinal spread of a more distant tumor can cause **superior vena cava (SVC) syndrome**, which is commonly associated with small cell lung carcinoma. SVC syndrome causes headache, facial and upper-extremity edema, and dilated veins of the upper torso.


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**cava (SVC) syndrome**, which is commonly associated with small cell lung carcinoma. SVC syndrome causes headache, facial and upper-extremity edema, and dilated veins of the upper torso.

- Involvement of the recurrent laryngeal nerve may cause hoarseness.
- Dysphagia may result if the tumor compresses the esophagus.

**(Choice A)** The brainstem, which is the site of origin of most cranial nerves, contains the respiratory center (in the medulla oblongata) and is traversed by spinal tracts. Brainstem strokes typically present with vertigo and, in extreme cases, can lead to locked-in syndrome (spastic quadriplegia and paralysis of most cranial nerves with preserved consciousness).

**(Choice B)** C1 is unique among the spinal nerves in that it carries only motor fibers. C1-C3 lesions could affect neck musculature but would not explain this patient's hiccups or dyspnea.

**Educational objective:**
The phrenic nerve arises from the C3-C5 segments of the spinal cord and innervates the ipsilateral hemidiaphragm. Intrathoracic spread of lung cancer may affect the phrenic nerve, causing hiccups and diaphragmatic paralysis with dyspnea. Brachial plexus involvement can cause pain in the distribution of the C8, T1, and T2 nerve roots. Involvement of the recurrent laryngeal nerve may cause hoarseness.


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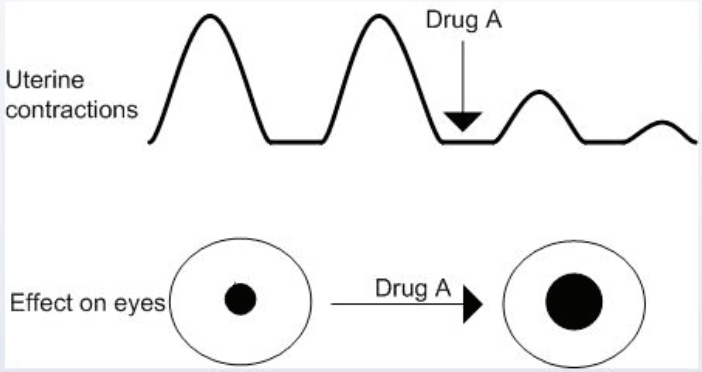
A medical student is observing a pharmacology experiment where drug A is being intravenously administered to a pregnant dog. Some parameters that are being recorded during the experiment include heart rate, blood pressure, pupil size, and uterine contractions. The following diagrams illustrate the measured parameters and observed changes after infusing drug A.




Which of the following best characterizes drug A?

A. Beta-adrenergic agonist

B. Alpha and beta-adrenergic agonist



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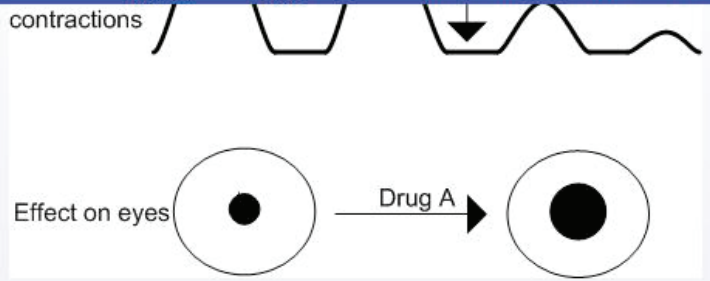


Which of the following best characterizes drug A?

A. Beta-adrenergic agonist

B. Alpha and beta-adrenergic agonist

C. Alpha-adrenergic agonist

D. Beta-adrenergic antagonist

E. Alpha-adrenergic antagonist and beta-adrenergic agonist

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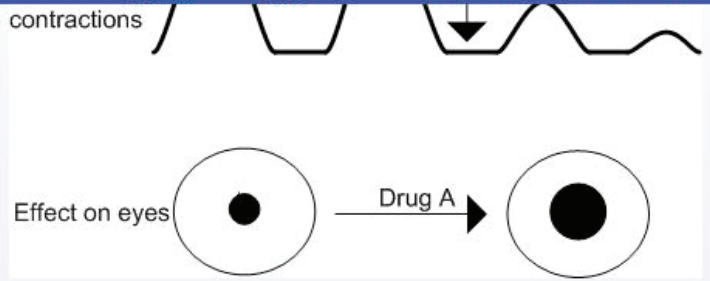


Which of the following best characterizes drug A?

- A. Beta-adrenergic agonist (17%)
- ✓ B. Alpha and beta-adrenergic agonist (43%)
- C. Alpha-adrenergic agonist (15%)
- D. Beta-adrenergic antagonist (7%)
- E. Alpha-adrenergic antagonist and beta-adrenergic agonist (15%)

Correct

43%
Answered correctly

51 secs
Time Spent

01/30/2021
Last Updated



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Although the most pronounced effects of adrenergic agonists are those on the heart and vasculature, these drugs also affect many other organs. The graph above illustrates the effects of adrenergic stimulation on the eye and uterus. The pupillary dilator muscle of the eye possesses α1 receptors, and the stimulation of these α1 receptors results in contraction of the pupillary dilator muscle with subsequent dilation of the pupil (mydriasis). Ophthalmic preparation of phenylephrine (selective α-adrenergic agonist) is used to dilate the pupil before ophthalmoscopic examination.

Adrenergic receptors of the uterus belong to the β2 group whose stimulation leads to uterine relaxation (an effect called tocolysis) which is used in obstetrics to defer premature labor. Adrenergic β2 agonists such as ritodrine and terbutaline are used for this purpose. The drug in question, therefore, displays both α and β-adrenergic effects. See the table for the summary of end-organ effects of adrenergic agonists.

| Receptor | Target organ | Effect of stimulation | Example |
|---|---|---|---|
| Alpha-1 | Peripheral vasculature<br>Bladder<br><br>Eye | ↑SBP<br>Contraction of internal urethral sphincter<br>Mydriasis (contraction of pupillary dilator muscle) | Epinephrine<br>Norepinephrine<br>Phenylephrine<br>Methoxamine |
| Beta-1 | Heart | ↑HR, contractility and | Epinephrine<br>Dopamine |


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β-adrenergic effects. See the table for the summary of end-organ effects of adrenergic agonists.

| Receptor | Target organ | Effect of stimulation | Example |
|---|---|---|---|
| Alpha-1 | Peripheral vasculature<br>Bladder<br><br>Eye | ↑SBP<br>Contraction of internal urethral sphincter<br>Mydriasis (contraction of pupillary dilator muscle) | Epinephrine<br>Norepinephrine<br>Phenylephrine<br>Methoxamine |
| Beta-1 | Heart | ↑HR, contractility and conductance | Epinephrine<br>Dopamine<br>Dobutamine<br>Isoproterenol |
| Beta-2 | Peripheral vasculature (skeletal muscle)<br>Bronchi<br>Uterus | Vasodilatation, ↓DBP<br><br>Bronchodilatation<br>Relaxation (tocolysis) | Isoproterenol<br>Terbutaline<br>Ritodrine |

**(Choice A)** Beta-adrenergic agonists stimulate β2-adrenergic receptors of the uterus and diminish uterine contractions. They do not, however, affect α1-receptors of the eye and would not produce mydriasis.

**(Choice C)** Alpha-adrenergic agonists would produce mydriasis (α1 effect), but not uterine relaxation (β2 effect).

**(Choice D)** Beta-adrenergic antagonists block β2 receptors of the uterus and enhance uterine contraction. They do not affect α1-adrenoreceptors of the pupillary dilator of the eye.



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**(Choice A)** Beta-adrenergic agonists stimulate β2-adrenergic receptors of the uterus and diminish uterine contractions. They do not, however, affect α1-receptors of the eye and would not produce mydriasis.

**(Choice C)** Alpha-adrenergic agonists would produce mydriasis (α1 effect), but not uterine relaxation (β2 effect).

**(Choice D)** Beta-adrenergic antagonists block β2 receptors of the uterus and enhance uterine contraction. They do not affect α1-adrenoreceptors of the pupillary dilator of the eye.

**(Choice E)** Alpha-adrenergic antagonist and beta-adrenergic agonist would cause miosis (pupillary constriction) and uterine relaxation.

**Educational Objective:**
Inhibition of uterine contractions (tocolysis) is a result of β2 adrenergic receptor stimulation. Alpha -1 receptor stimulation causes contraction of the ocular pupillary dilator muscle, resulting in mydriasis (pupillary dilation).

| Pharmacology | Nervous System | Sympathomimetic agents |
|---|---|---|
| Subject | System | Topic |


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An 8-year-old male with a long history of recurrent pulmonary infections is being evaluated for some neurological symptoms. His gait is unsteady, and he has been known to spontaneously lose his balance and fall. The parents are concerned about their son's language development, as they do not feel that he is progressing appropriately. Additionally, the patient's father states that the child's eyes and head "do not move smoothly" when he is looking at moving objects. Physical examination also reveals numerous superficial blanching nests of distended capillaries on sun-exposed areas of his skin. The genetic defect in this child most likely plays a role in:

A. Mitochondrial iron transport
B. DNA break repair
C. Purine catabolism
D. HLA class II antigen expression
E. Sphingolipid degradation

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An 8-year-old male with a long history of recurrent pulmonary infections is being evaluated for some neurological symptoms. His gait is unsteady, and he has been known to spontaneously lose his balance and fall. The parents are concerned about their son's language development, as they do not feel that he is progressing appropriately. Additionally, the patient's father states that the child's eyes and head "do not move smoothly" when he is looking at moving objects. Physical examination also reveals numerous superficial blanching nests of distended capillaries on sun-exposed areas of his skin. The genetic defect in this child most likely plays a role in:

- A. ~~Mitochondrial iron transport~~ (6%)
- ✓ B. DNA break repair (61%)
- C. ~~Purine catabolism~~ (7%)
- D. ~~HLA class II antigen expression~~ (8%)
- E. Sphingolipid degradation (15%)


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Cerebellar ataxia, telangiectasias, and increased risk of sinopulmonary infections constitute a characteristic triad of ataxia telangiectasia. Telangiectasias are described clinically exactly as they are in the question stem - superficial blanching nests of distended capillaries. Ataxia-telangiectasia also predisposes to an increased risk of hematologic malignancies and causes an immune deficiency consisting of both cell-mediated and humoral dysfunction. The immune deficiency primarily manifests as an IgA deficiency and predisposes to infections of the upper and lower airways.

It is an autosomal recessive condition that occurs due to mutation of ATM gene. ATM (**A**taxia **T**elangiectasia **M**utated) gene is responsible for DNA break repair. DNA in patients with ataxia-telangiectasia is hypersensitive to X-ray radiation that causes multiple chromosomal breaks.

**(Choice A)** Mitochondrial iron transport is important for heme synthesis. It is inhibited by lead; this is one of the reasons why lead intoxications causes hypochromic anemia.

**(Choice C)** An example of a disease that results from defective purine catabolism is Lesch-Nyhan syndrome. This is an X-linked recessive disorder that results from a defect in the gene coding for hypoxanthine-guanine phosphoribosyltransferase (HGPRT). This defect leads to a severe hyperuricemia and gout. Of note, these patients classically exhibit self-mutilating behavior in addition to mental


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retardation, choreoathetoid movements and spasticity.

**(Choice D)** Bare lymphocyte syndrome is an immunodeficiency resulting from a defect in expression of HLA class II antigens on the surfaces of antigen presenting cells. MHC Class II is needed to present foreign antigen to T cells to elicit a cell mediated AND a humoral response (because T cells must first activate B cells to mature and undergo class switching).

**(Choice E)** Sphingolipid degradation is defective in Niemann-Pick disease. This disease is caused by an autosomal recessive defect in sphingomyelinase and results in accumulation of sphingomyelin within monocytic cells leading to death in early childhood. Signs and symptoms of disease include hepatosplenomegaly, anemia, motor neuropathy leading to hypotonia and areflexia, and a "cherry red spot" on the macula (not unlike that of Tay-Sachs disease).

**Educational objective:**
Cerebellar ataxia, telangiectasias, and increased risk of sinopulmonary infections constitute a characteristic triad of ataxia telangiectasia. This illness exhibits autosomal recessive inheritance, and the defect is in a gene that codes for the "ATM" gene which plays a role in DNA break repair. The immune deficiency primarily manifests as an IgA deficiency and predisposes to infections of the upper and lower airways.

**References**


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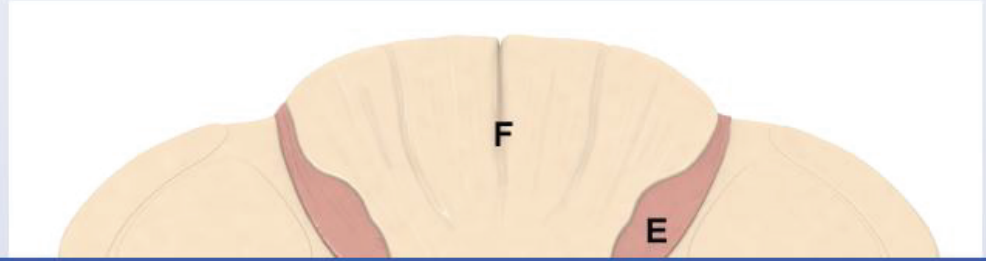
A 20-year-old woman comes to the physician because of multiple burns on her hands. She says that she gets burned quite often when she cooks, particularly while operating the oven. She also has burned herself when picking up her morning cup of coffee and when testing the water temperature in the shower. The patient is concerned because she cannot feel when objects are "really hot" and often does not notice that she has burns until she looks at her hands. She has no significant past medical history, no recent illnesses, and no sick contacts. Her surgical history is significant only for removal of impacted wisdom teeth 1 year ago. The patient has never smoked, drinks alcohol occasionally, and does not use illicit drugs. Her family history is significant for multiple sclerosis in her mother. Examination shows diminished pinprick and temperature sensation across the upper back, shoulders, and arms bilaterally. Light touch, position, and vibration sense are preserved. Examination of the lower extremities is unremarkable. Damage to which of the following spinal cord areas is most likely responsible for this patient's symptoms?



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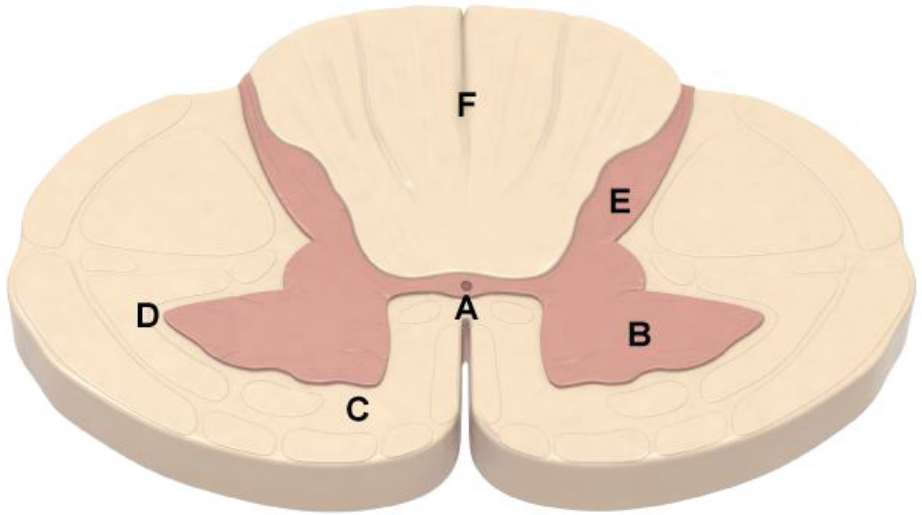


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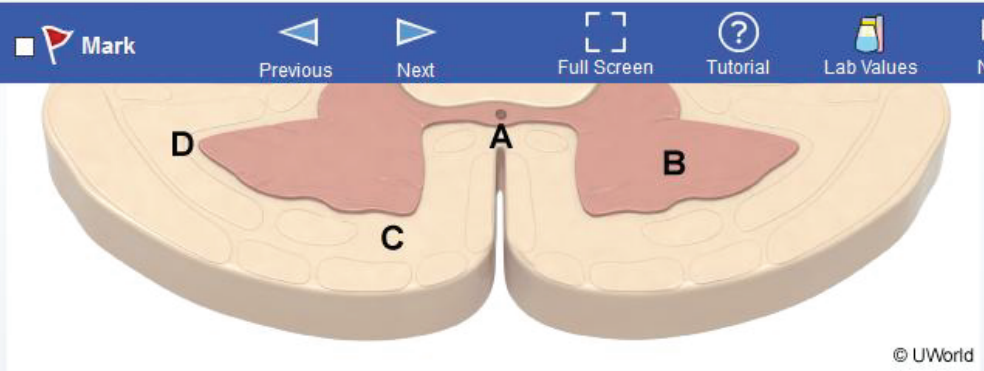


- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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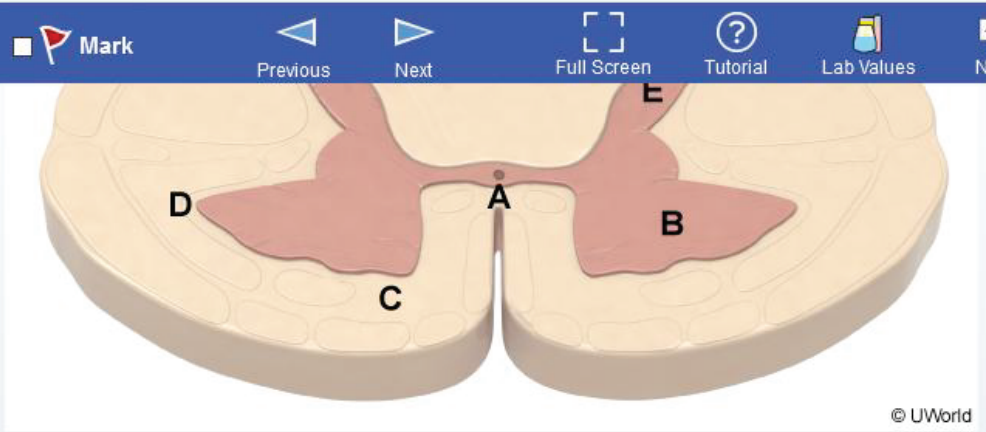
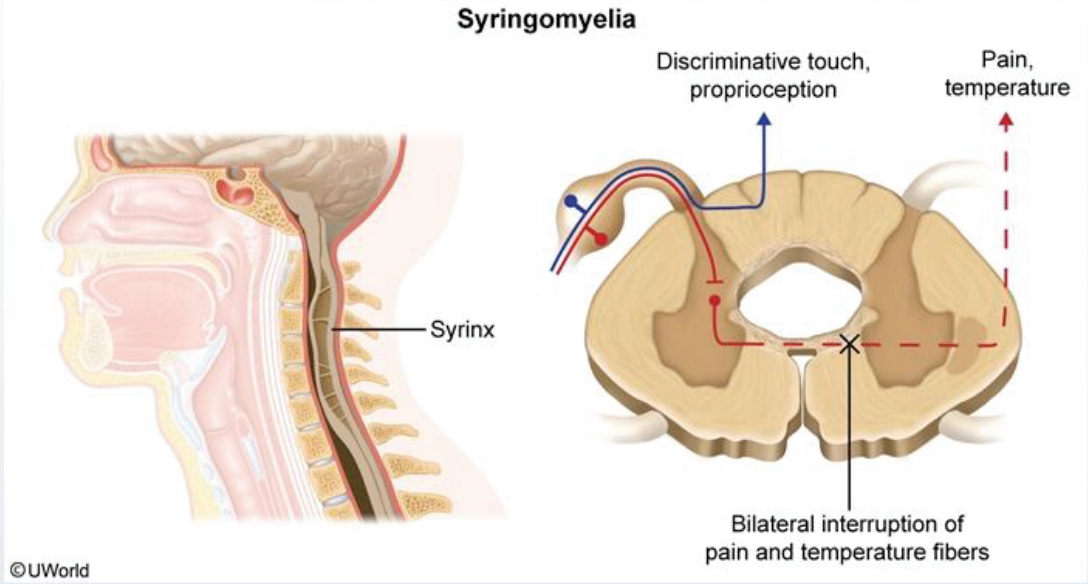



- A. A (62%)
- B. B (3%)
- C. C (8%)
- D. D (14%)
- E. E (5%)
- F. F (5%)




This patient most likely has **syringomyelia**, which classically presents with disproportionate **loss of pain and temperature sensation** (dissociated anesthesia) involving the **arms and hands**. In syringomyelia, a cerebrospinal fluid-filled cavity called a syrinx usually forms in the cervical region of the spinal cord. These cavities can enlarge over time and destroy adjacent portions of the spinal cord. The areas most commonly damaged are the ventral white commissure and ventral horns.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damaged are the ventral white commissure and ventral horns.

The ventral white commissure is located just anterior to the gray commissure. It is the area of decussation for the fibers of the lateral spinothalamic tract, which transmits pain and temperature sensation from peripheral receptors to the somatosensory cortex. Destruction of the **ventral white commissure** leads to loss of pain and temperature sensation bilaterally over the affected dermatomes (starting 1 to 2 levels below the lesion, as the axons briefly ascend in the zone of Lissauer before decussating). Touch, vibration, and position senses are preserved as the dorsal columns remain intact.

**(Choice B)** The **ventral horns** contain lower motor neurons that receive impulses from the lateral corticospinal tract. Damage to the ventral horn can occur in syringomyelia, but would cause flaccid paralysis and atrophy of the intrinsic hand muscles (not loss of pain and temperature sensation).

**(Choice C)** The ventral spinothalamic tract is located in this area and transmits crude touch and pressure sensation. It should not be confused with the lateral spinothalamic tract, which carries pain and temperature sensation.

**(Choice D)** After decussating in the ventral white commissure, axons of the lateral spinothalamic tract ascend to the brain in the lateral funiculus. Damage to this area would cause contralateral loss of pain and temperature sensation distally, beginning 1 to 2 segments below the lesion. However, bilateral sensory



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damaged are the ventral white commissure and ventral horns.

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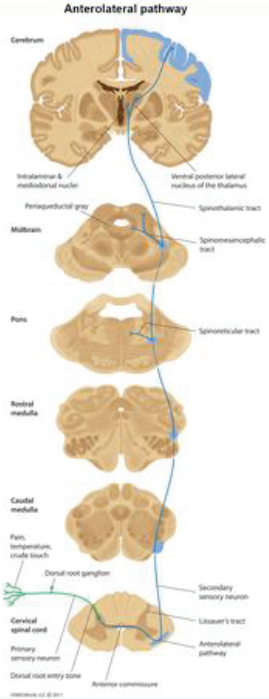


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ascend to the brain in the lateral funiculus. Damage to this area would cause contralateral loss of pain and temperature sensation distally, beginning 1 to 2 segments below the lesion. However, bilateral sensory loss would not occur with damage to this area.

**(Choice E)** The dorsal horn contains first order axons and second order neurons that transmit sensory input from peripheral receptors. Damage to the dorsal horn would likely result in unilateral loss of all sensation over the affected dermatomes.

**(Choice F)** The dorsal column contains both the gracile and cuneate fasciculi. They are formed by axons of first-order neurons of the dorsal column pathway. This tract is the primary mediator of proprioception, vibration, and tactile sensation.

**Educational objective:**
Syringomyelia is characterized by the formation of a cavity (syrinx) in the cervical region of the spinal cord. The syrinx damages the ventral white commissure, leading to bilateral loss of pain and temperature sensation that is limited to the affected levels (typically the arms and hands); distal sensation is preserved. Destruction of the motor neurons in the ventral horns (due to extension of the syrinx) results in flaccid paralysis and atrophy of the intrinsic muscles of the hand.

**References**


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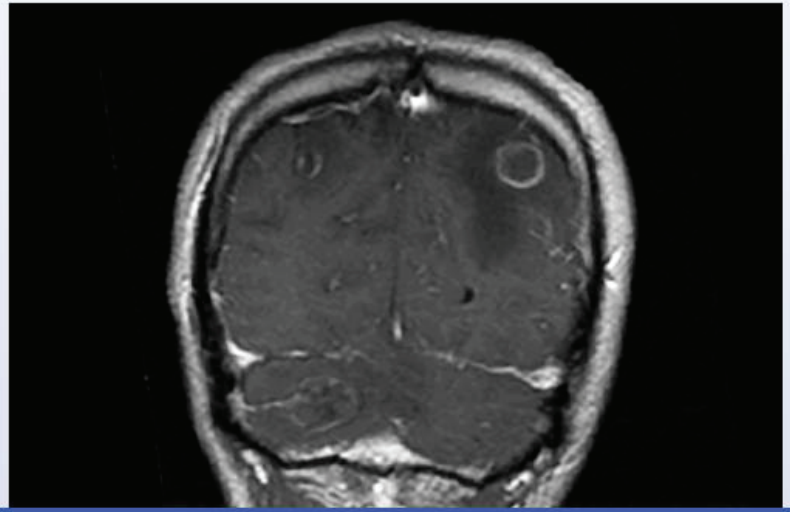
A 42-year-old man is brought to the emergency department following an episode of generalized tonic-clonic seizure witnessed by his family. He has no prior history of seizure but has had headaches for the past several weeks. The patient works in construction. He has no history of travel outside the United States and has never had any pets. He smokes a pack of cigarettes daily and drinks 3-4 cans of beer every evening. Physical examination is notable for a postictal state, oral thrush, and several enlarged cervical and inguinal lymph nodes. An MRI of his brain with contrast is shown in the image below.





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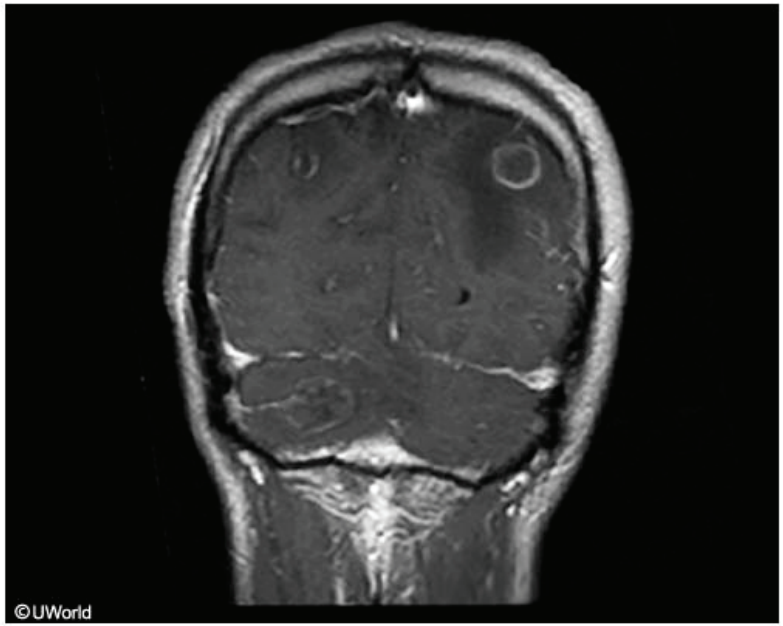


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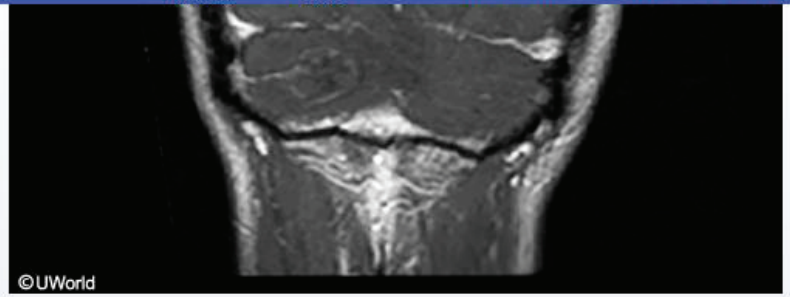


Which of the following is the most likely cause of this patient's symptoms?

A. *Aspergillus fumigatus*
B. Glioblastoma multiforme
C. *Mycobacterium tuberculosis*
D. Neurocysticercosis
E. Toxoplasmosis

Submit



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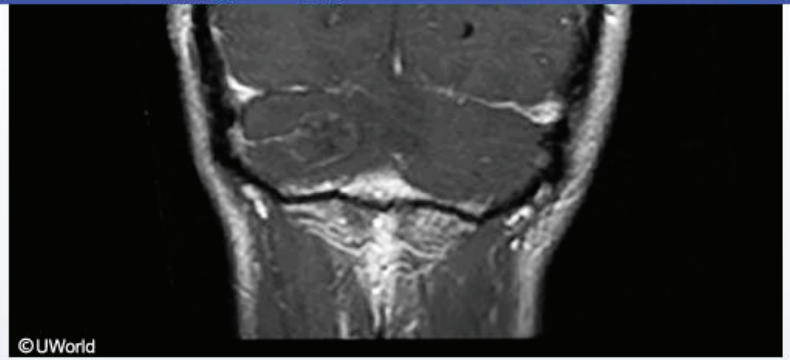


Which of the following is the most likely cause of this patient's symptoms?

A. *Aspergillus fumigatus* (13%)

B. Glioblastoma multiforme (4%)

C. *Mycobacterium tuberculosis* (2%)

D. Neurocysticercosis (14%)

E. Toxoplasmosis (65%)



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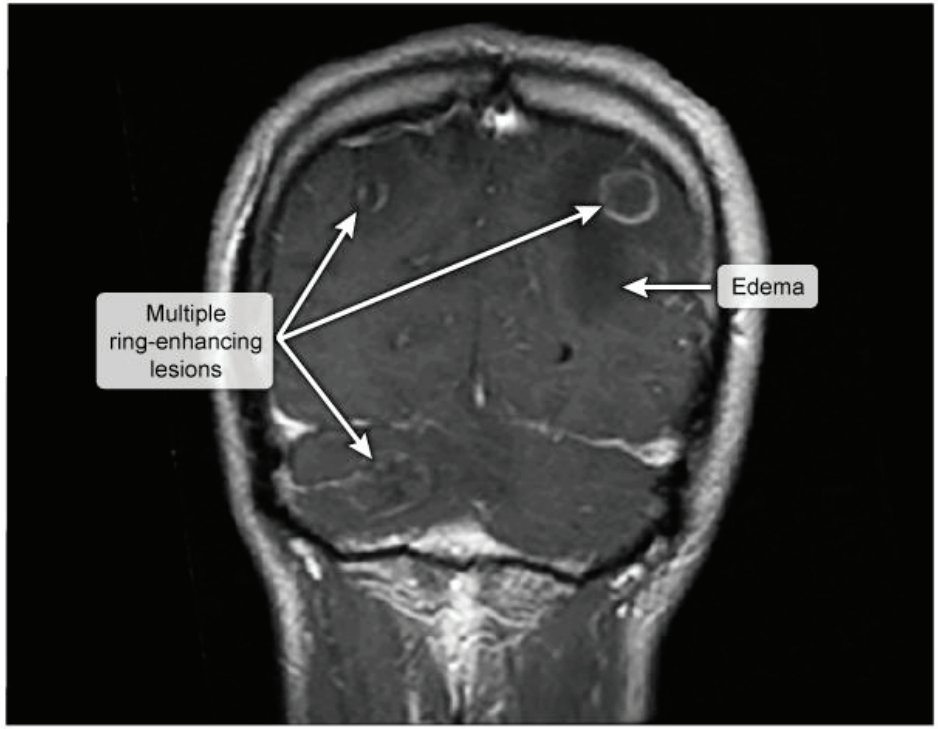
## Toxoplasma encephalitis

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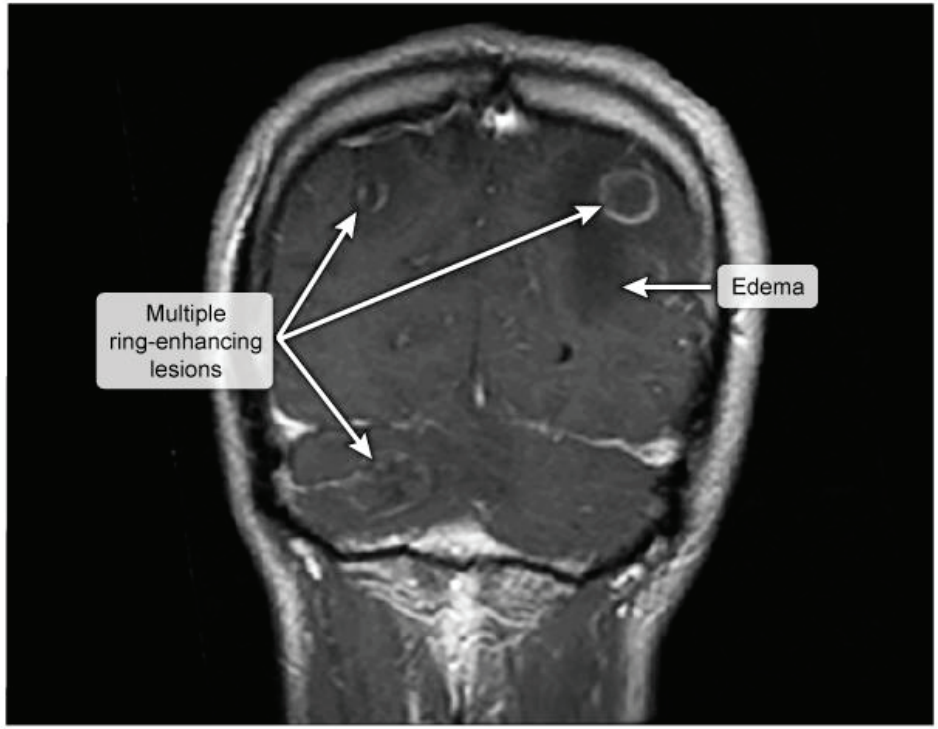
## Toxoplasma encephalitis

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This patient likely has **HIV** given his oral thrush (usually seen with CD4 count <200/mm$^3$), cervical and inguinal lymphadenopathy, and brain lesions. In patients with HIV (particularly those with low CD4 counts), headaches, **seizures**, and **multiple ring-enhancing** central nervous system (CNS) lesions on MRI (white arrows) suggest **toxoplasmic encephalitis**. Seizures are a common complication of such brain lesions and their surrounding edema. Extensive pet (cat) exposure is not essential for the diagnosis, as toxoplasmosis can also be transmitted through contaminated foods.

**(Choice A)** *Aspergillus* is not a leading opportunistic pathogen in patients with HIV, possibly because they have relatively intact phagocytic function despite their T cell dysfunction. *Aspergillus* typically affects the lungs; however, it can cause brain abscesses in patients who are immunocompromised due to neutropenia or transplant.

**(Choice B)** Although CNS glioblastomas are ring-enhancing, they are typically solitary and often have a characteristic butterfly appearance.

**(Choices C and D)** Neurocysticercosis (due to *Taenia solium* [pork tapeworm] ingestion) can cause multiple brain lesions but would be unlikely in this patient with no travel history to South or Central America. Similarly, *Mycobacterium tuberculosis* CNS infection, which can cause similar lesions, is a consideration in developing countries but is a less likely diagnosis in the United States.



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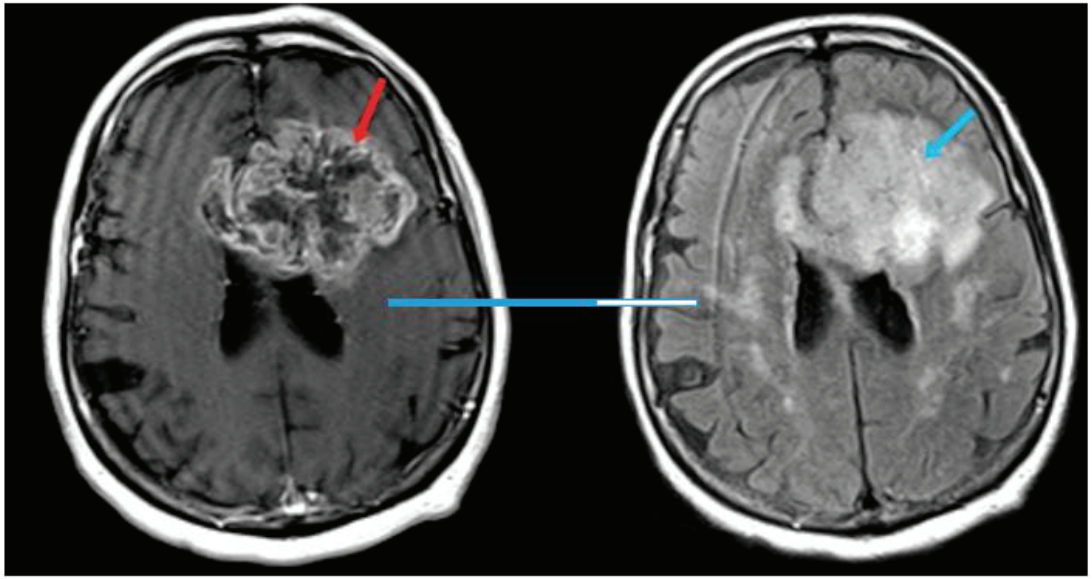

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**(Choice A)** *Aspergillus* is not a leading opportunistic pathogen in patients with HIV, possibly because they have relatively intact phagocytic function despite their T cell dysfunction. *Aspergillus* typically affects the lungs; however, it can cause brain abscesses in patients who are immunocompromised due to neutropenia or transplant.

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**Educational objective:**
The finding of multiple ring-enhancing lesions in an HIV patient is most likely due to toxoplasmosis.

| Microbiology | Nervous System | Toxoplasmosis |
|---|---|---|
| Subject | System | Topic |

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An 82-year-old woman comes to the clinic due to memory loss. She lives with her daughter, who reports that her mother has had difficulty remembering recent conversations. The patient has also forgotten recent events, such as her grandson's birthday party last month. Two years ago, she was forced to give up driving after repeatedly getting lost in her own neighborhood and being involved in a minor motor vehicle accident. The patient still enjoys reminiscing about old times with friends and playing bingo at church. The daughter now manages her mother's finances and acts as her health care proxy. Which of the following is the most likely pathological finding in this patient?

A. Demyelinated plaques
B. Large intracytoplasmic vacuoles
C. Lewy bodies
D. Multiple lacunar infarcts
E. Negri bodies
F. Neuritic plaques


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that her mother has had difficulty remembering recent conversations. The patient has also forgotten recent events, such as her grandson's birthday party last month. Two years ago, she was forced to give up driving after repeatedly getting lost in her own neighborhood and being involved in a minor motor vehicle accident. The patient still enjoys reminiscing about old times with friends and playing bingo at church. The daughter now manages her mother's finances and acts as her health care proxy. Which of the following is the most likely pathological finding in this patient?

A. ~~Demyelinated plaques~~ (4%)
B. ~~Large intracytoplasmic vacuoles~~ (3%)
C. ~~Lewy bodies~~ (11%)
D. ~~Multiple lacunar infarcts~~ (3%)
E. ~~Negri bodies~~ (1%)
✓ F. Neuritic plaques (75%)

Correct
75%
53 secs
11/24/2020


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This elderly patient likely has Alzheimer dementia, a neurodegenerative disorder that presents insidiously with **memory loss**, especially of **recent events**. Other cognitive deficits such as **executive dysfunction** (eg, difficulty planning and organizing) and **visuospatial impairment** (eg, getting lost in one's own neighborhood) may also occur early in the disease course, whereas language and behavioral abnormalities often appear later.

Classic histopathologic findings of Alzheimer disease include amyloid plaques and neurofibrillary tangles. Neuritic (senile) plaques are extracellular deposits often found in the medial temporal lobe (eg, hippocampus, amygdala, entorhinal cortex) and are composed of a central amyloid beta (Aβ) core surrounded by dystrophic neurites. Abnormal accumulation of Aβ is toxic to neurons and is thought to occur secondary to impaired clearance or overproduction of amyloid precursor protein. Neurofibrillary tangles are found in the neuronal cytoplasm and consist of aggregates of hyperphosphorylated tau protein, which normally mediates microtubule stabilization.

**(Choice A)** Demyelinated plaques are seen in multiple sclerosis, which typically presents in young to middle-age adults with neurologic deficits disseminated in space and time.

**(Choice B)** Large intracytoplasmic vacuoles, sometimes described as spongiform, are seen in prion diseases such as Creutzfeldt-Jakob disease. This condition typically presents with rapidly progressive


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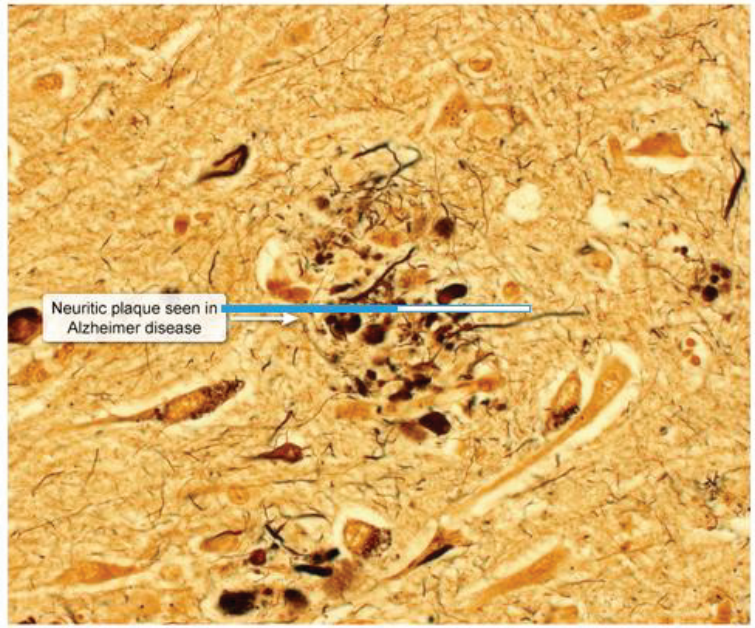
Alzheimer disease

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diseases such as Creutzfeldt-Jakob disease. This condition typically presents with rapidly progressive



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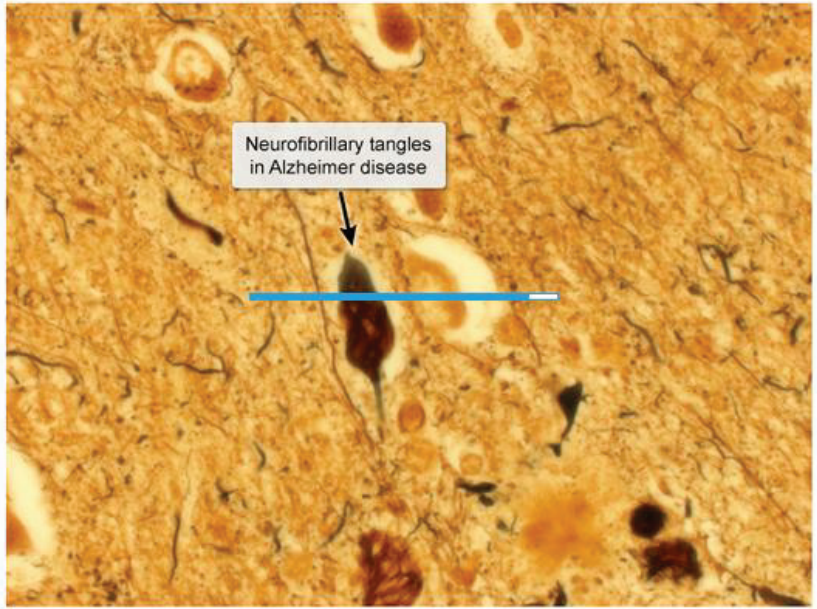
Alzheimer disease

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diseases such as Creutzfeldt-Jakob disease. This condition typically presents with rapidly progressive



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middle-age adults with neurologic deficits disseminated in space and time.

**(Choice B)** Large intracytoplasmic vacuoles, sometimes described as spongiform, are seen in prion diseases such as Creutzfeldt-Jakob disease. This condition typically presents with rapidly progressive dementia and myoclonus.

**(Choice C)** Lewy bodies are intracellular eosinophilic inclusions composed of α-synuclein that are typically seen in patients with Parkinson disease and Lewy body dementia. Lewy body dementia classically presents with attention deficits, visual hallucinations, and spontaneous parkinsonism (eg, bradykinesia, rigidity, resting tremor).

**(Choice D)** Multiple lacunar infarcts would be expected in vascular dementia. Vascular dementia is distinguished from Alzheimer dementia by a step-wise rather than gradual decline in cognitive function, as well as focal neurologic deficits.

**(Choice E)** Negri bodies are round eosinophilic inclusions seen in the cytoplasm of pyramidal hippocampal neurons and cerebellar Purkinje cells in patients infected with the rabies virus.

**Educational objective:**
Alzheimer dementia typically presents insidiously with memory loss (especially of recent events), executive dysfunction, and visuospatial impairment. Classic histopathologic findings include amyloid plaques (central


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**(Choice C)** Lewy bodies are intracellular eosinophilic inclusions composed of α-synuclein that are typically seen in patients with Parkinson disease and Lewy body dementia. Lewy body dementia classically presents with attention deficits, visual hallucinations, and spontaneous parkinsonism (eg, bradykinesia, rigidity, resting tremor).

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**(Choice E)** Negri bodies are round eosinophilic inclusions seen in the cytoplasm of pyramidal hippocampal neurons and cerebellar Purkinje cells in patients infected with the rabies virus.

**Educational objective:**
Alzheimer dementia typically presents insidiously with memory loss (especially of recent events), executive dysfunction, and visuospatial impairment. Classic histopathologic findings include amyloid plaques (central amyloid beta core surrounded by dystrophic neurites) and neurofibrillary tangles (aggregates of hyperphosphorylated tau protein).

**References**

- Pathogenesis of Alzheimer's disease.



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A 60-year-old farmer is brought to the emergency department due to acute-onset confusion, muscle weakness, and difficulty breathing. The patient has vomited twice and has had 3 loose bowel movements over the past 2 hours. His medical history is insignificant and he currently takes no medications. Blood pressure is 110/70 mm Hg, pulse is 58/min, and respirations are 26/min. His pupils are constricted, symmetric, and reactive to light. Examination reveals excessive sweating, lacrimation, and wheezing. He is incontinent of urine. Intravenous atropine is administered. Which of the following findings is most likely to persist in this patient without additional therapy?

A. Bradycardia
B. Bronchospasm
C. Diarrhea
D. Miosis
E. Muscle weakness
F. Urinary incontinence


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A. Bradycardia (6%)
B. Bronchospasm (11%)
C. Diarrhea (4%)
D. Miosis (11%)
✓ E. Muscle weakness (59%)
F. Urinary incontinence (7%)

Correct

59%
38 secs
01/15/2021



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| Cholinergic toxicity | |
|---|---|
| Muscarinic effects **(DUMBELS)** | • **D**iarrhea/diaphoresis<br>• **U**rination<br>• **M**iosis<br>• **B**ronchospasm, bronchorrhea & bradycardia<br>• **E**mesis<br>• **L**acrimation<br>• **S**alivation |
| Nicotinic effects | • Muscle weakness, paralysis & fasciculations |

This farmer is exhibiting multiple signs of excessive cholinergic stimulation. He has likely been exposed to an **organophosphate**, a **cholinesterase inhibitor** that is commonly used in agricultural pesticides. Organophosphates inhibit cholinesterase in both muscarinic and nicotinic cholinergic synapses, leading to decreased acetylcholine degradation. Overabundance of acetylcholine within the synaptic cleft leads to overstimulation of the corresponding receptors.

This patient is currently experiencing the effects of widespread muscarinic activation, which increases


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This patient is currently experiencing the effects of widespread muscarinic activation, which increases visceral smooth muscle tone and glandular secretions throughout the body (**DUMBELS** mnemonic). Nicotinic activation leads to muscle fasciculations, weakness, and paralysis. Activation of both receptors in the central nervous system leads to seizures and coma. Atropine is a competitive inhibitor of acetylcholine at the muscarinic receptors, thereby reversing muscarinic symptoms of organophosphate poisoning. However, atropine has no effect on nicotinic receptors; patients are still at risk of **muscle paralysis**. **Pralidoxime** is a cholinesterase-reactivating agent that allows for degradation of excess acetylcholine and treats both the muscarinic and nicotinic effects of organophosphates.

**(Choices A, B, C, D and F)** Bradycardia, bronchospasm, diarrhea, miosis, and urinary incontinence are symptoms of excessive muscarinic activation, and are reversed with atropine.

**Educational objective:**
Organophosphates inhibit cholinesterase in both muscarinic and nicotinic cholinergic synapses, leading to decreased acetylcholine degradation and overstimulation of the corresponding receptors. Atropine reverses muscarinic effects but does not prevent the development of nicotinic effects such as muscle paralysis. Pralidoxime is a cholinesterase-reactivating agent that allows for degradation of excess acetylcholine and treats both the muscarinic and nicotinic effects of organophosphates.


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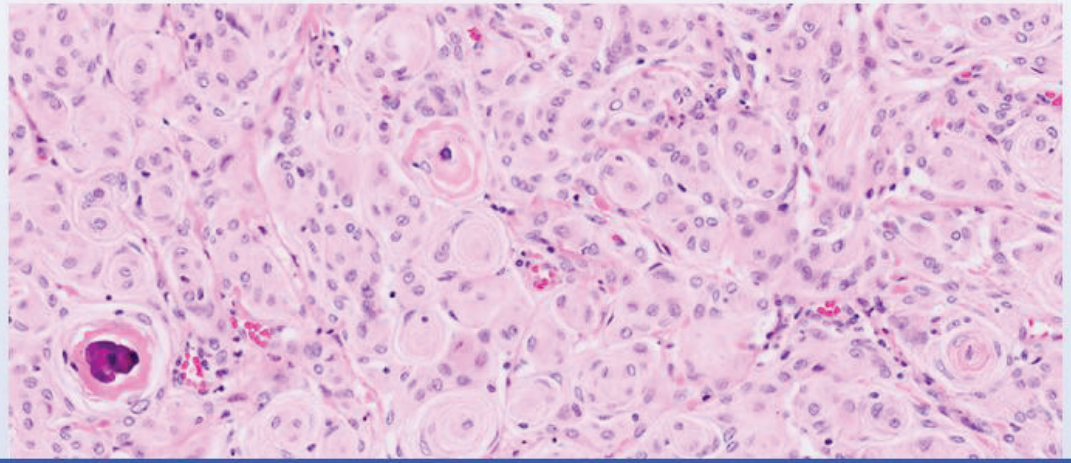
A 45-year-old woman is brought to the emergency department after an episode during which she abruptly lost consciousness and had rhythmic jerking movements of the limbs followed by a period of confusion. The patient has had mild daily headaches associated with nausea that have progressed over the past 2 years. The headaches are worse at night and occasionally awaken her. The patient reports no head trauma, visual changes, weakness, numbness, or difficulty swallowing or speaking. She does not use alcohol or illicit drugs. There is no family history of seizures. An intracranial mass is discovered on neuroimaging and a biopsy of the mass is shown in the image below.





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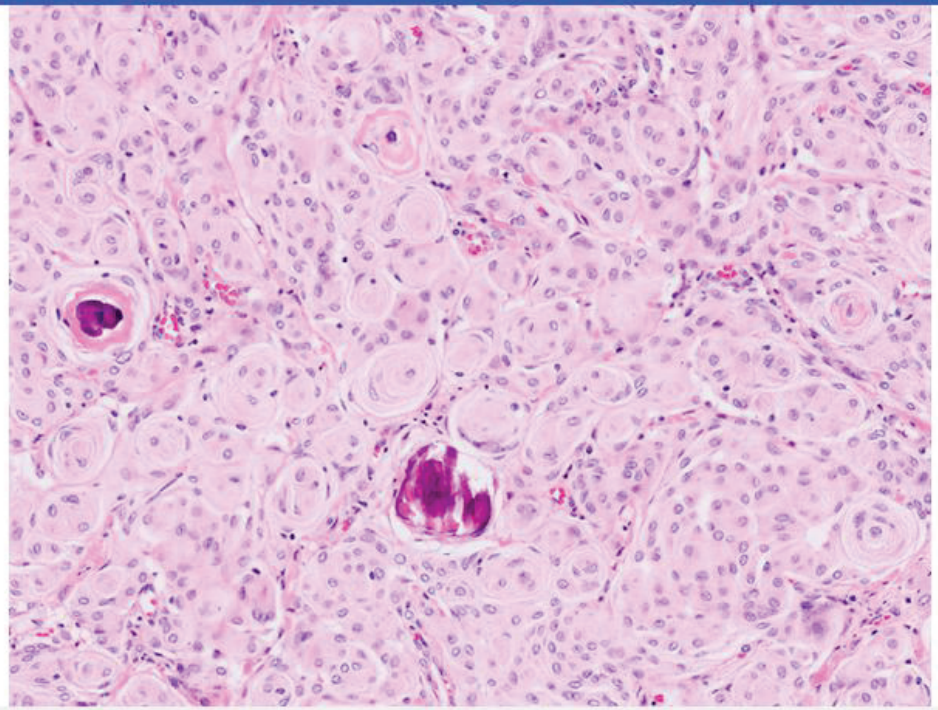

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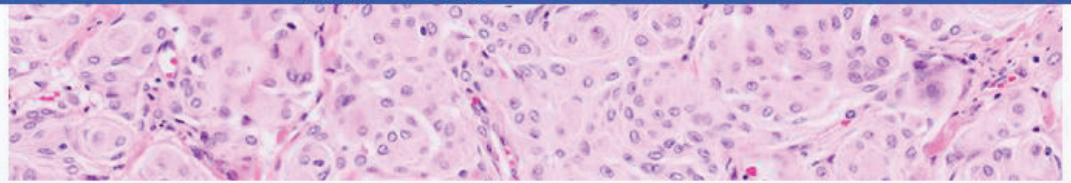

Which of the following is the most likely diagnosis?

- A. Craniopharyngioma
- B. Ependymoma
- C. Glioblastoma
- D. Medulloblastoma
- E. Meningioma
- F. Oligodendroglioma
- G. Pilocytic astrocytoma
- H. Schwannoma



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Which of the following is the most likely diagnosis?

- A. ~~Craniopharyngioma~~ (1%)
- B. Ependymoma (3%)
- C. ~~Glioblastoma~~ (6%)
- D. ~~Medulloblastoma~~ (3%)
- ✓ E. Meningioma (71%)
- F. ~~Oligodendroglioma~~ (7%)
- G. ~~Pilocytic astrocytoma~~ (2%)
- H. ~~Schwannoma~~ (3%)

Correct

71%
Answered correctly

01 min, 41 secs
Time Spent

03/01/2021
Last Updated



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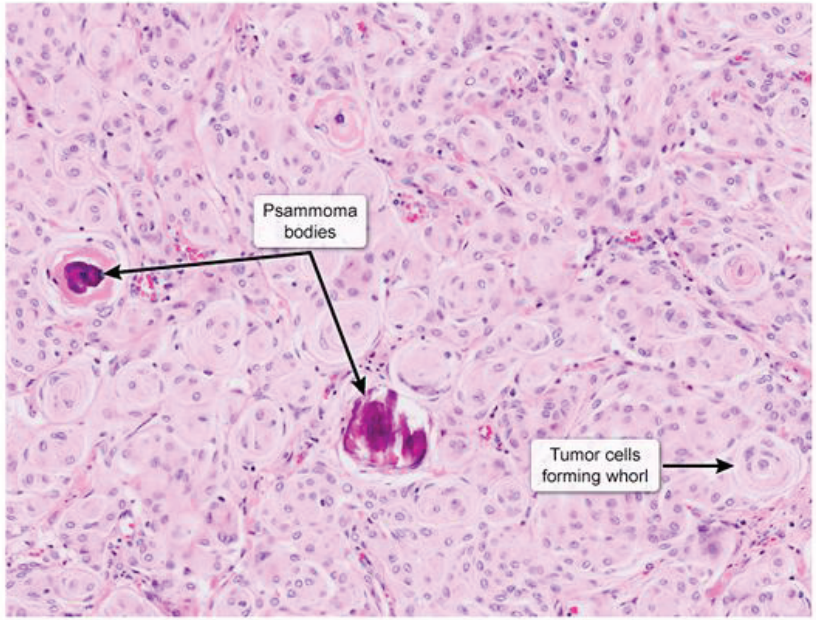
Meningioma

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This patient's biopsy findings are consistent with **meningioma**, a slow-growing benign tumor derived from meningothelial cells of the arachnoid. Note the syncytial nests and **whorled pattern** of cellular growth, which may calcify and appear as round, laminar structures called **psammoma bodies**. Other examples of tumors that form psammoma bodies include papillary thyroid carcinoma, mesothelioma, and serous carcinoma of the ovary and endometrium.

Meningiomas form well-circumscribed, round masses attached to the dura and are commonly found at the falcine, parasagittal, or lateral convexity regions of the brain. **Seizure** can occur due to compression of the adjacent cerebral cortex. Headaches, nausea, and vomiting may result from increased intracranial pressure, which worsens during recumbency and with sleep (due to increased intracranial blood volume). Individuals may also develop focal neurologic deficits depending on tumor size/location.

**(Choice A)** Adamantinomatous craniopharyngiomas most often present as benign suprasellar tumors in children and appear as cords/nests of palisading squamous epithelium with areas of lamellar "wet" keratin under light microscopy.

**(Choice B)** Ependymomas typically present as paraventricular tumors (eg, floor of the fourth ventricle) and have characteristic perivascular pseudorosettes under light microscopy.



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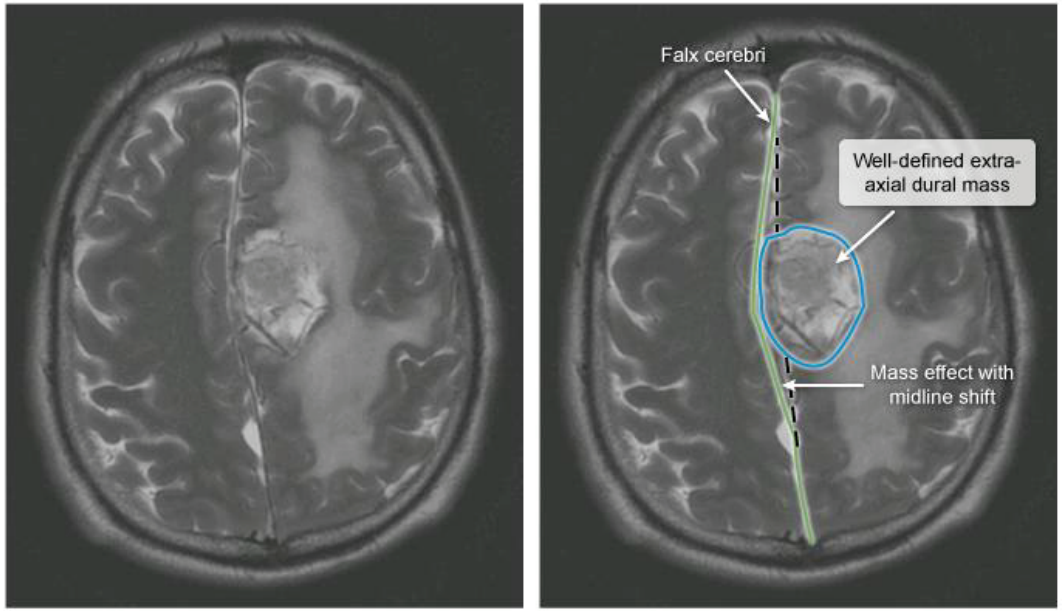
## Falcine meningioma

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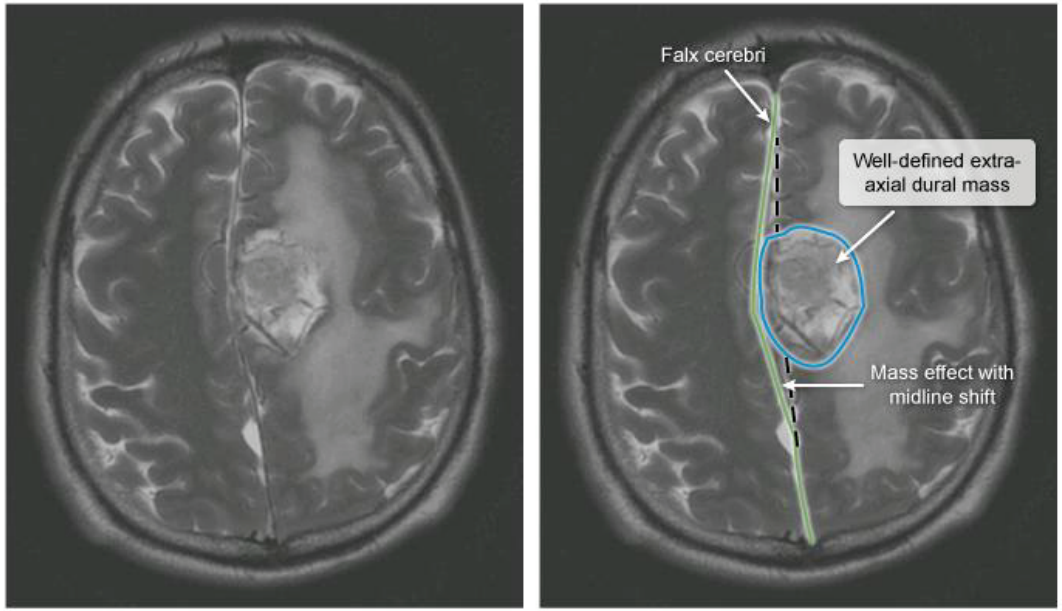
## Falcine meningioma

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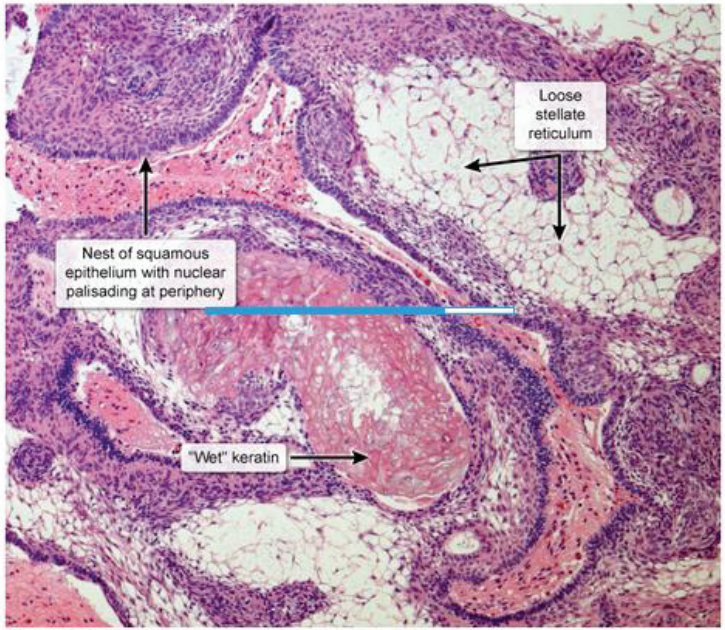
Adamantinomatous craniopharyngioma

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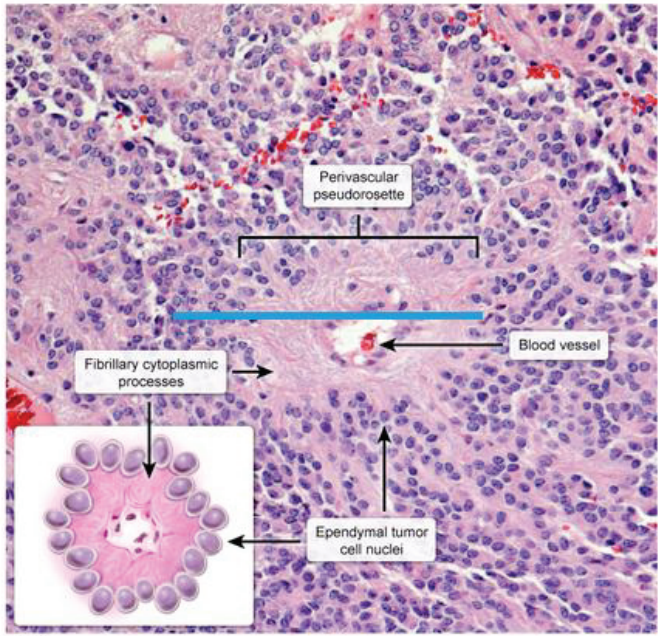
Ependymoma

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**(Choice C)** Glioblastomas are the most common primary malignant brain tumor in adults. They are often located in the cerebral hemispheres and may cross the corpus callosum ("butterfly glioma"). Light microscopy shows hypercellular areas of atypical astrocytes bordering regions of necrosis (pseudo-palisading).

**(Choice D)** Medulloblastomas are malignant cerebellar tumors that typically occur in children and are characterized by small blue cells that may surround neuropil (ie, interwoven nerve fibers and synapses), forming Homer Wright rosettes under light microscopy.

**(Choice F)** Oligodendrogliomas typically involve the white matter of the cerebral hemispheres, and tumor cells have a "fried egg" appearance (round nuclei surrounded by a halo of clear cytoplasm) under light microscopy.

**(Choice G)** Pilocytic astrocytomas are usually benign tumors that involve the cerebellum in children and young adults. Light microscopy typically shows tumor cells with elongated hairlike processes, eosinophilic granular bodies, and Rosenthal fibers.

**(Choice H)** Schwannomas are benign tumors that commonly arise from the vestibular branch of cranial nerve VIII at the cerebellopontine angle. Light microscopy typically shows spindle cells with palisading


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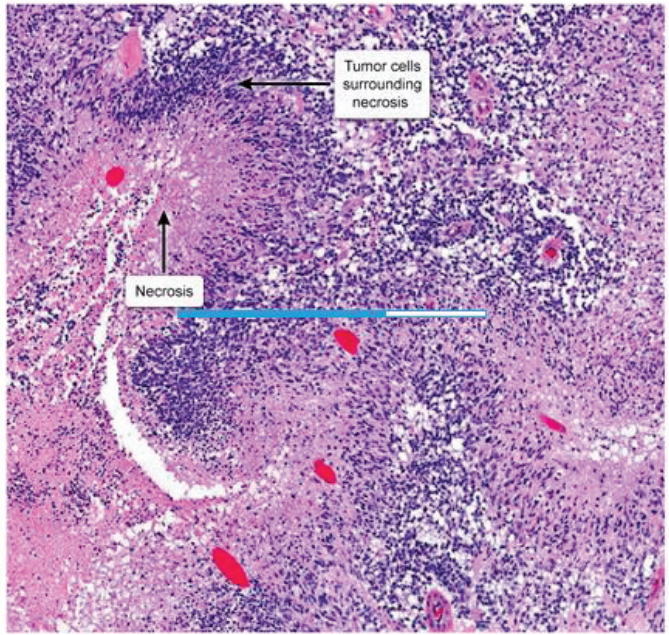
## Exhibit Display

**Glioblastoma**

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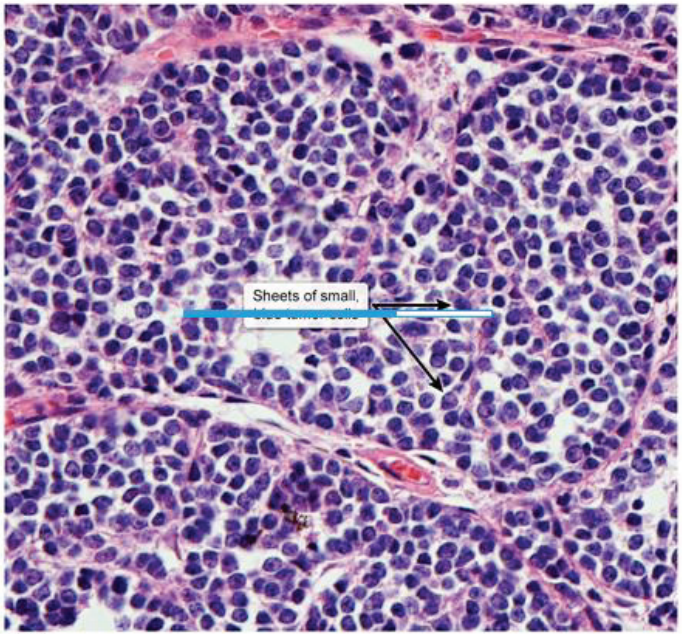
Medulloblastoma

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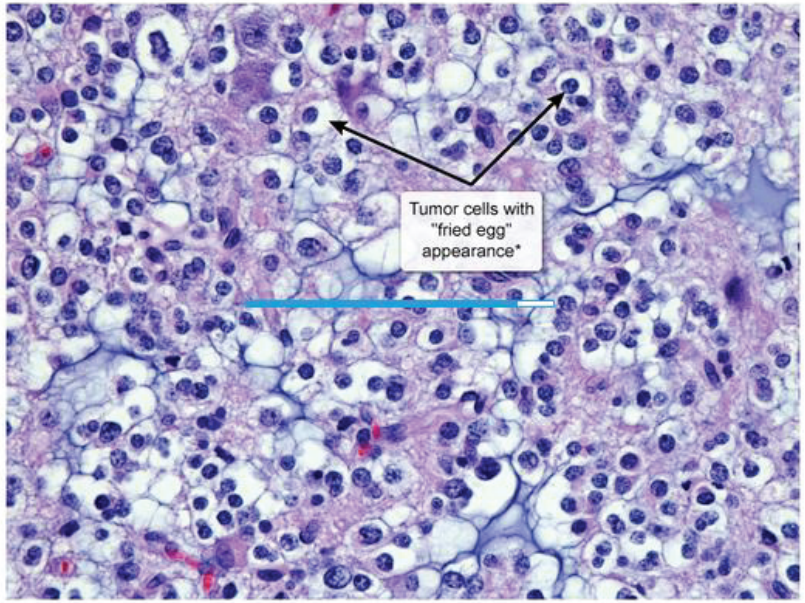
Oligodendroglioma




*Round nuclei with clear perinuclear halos

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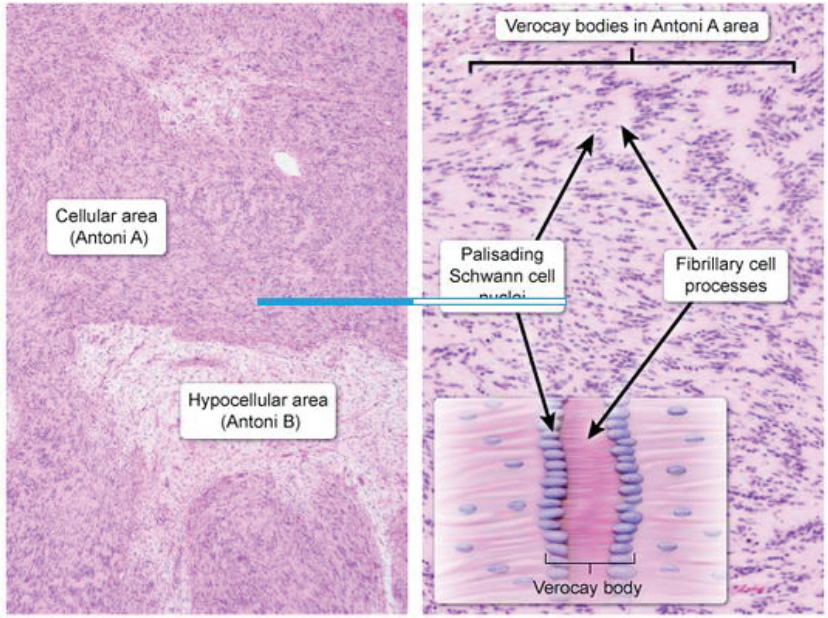
Schwannoma

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cells have a "fried egg" appearance (round nuclei surrounded by a halo of clear cytoplasm) under light microscopy.

**(Choice G)** Pilocytic astrocytomas are usually benign tumors that involve the cerebellum in children and young adults. Light microscopy typically shows tumor cells with elongated hairlike processes, eosinophilic granular bodies, and Rosenthal fibers.

**(Choice H)** Schwannomas are benign tumors that commonly arise from the vestibular branch of cranial nerve VIII at the cerebellopontine angle. Light microscopy typically shows spindle cells with palisading nuclei arranged around eosinophilic cores of fibrillary cell processes (Verocay bodies).

**Educational objective:**
Meningiomas are slow-growing, well-circumscribed, benign intracranial tumors typically found at the cerebral convexities in adults. Characteristic histopathologic features include syncytial nests and a whorled pattern of cellular growth, which may calcify into round, laminar structures called psammoma bodies.

| Pathology | Nervous System | Brain tumors |
|---|---|---|
| Subject | System | Topic |

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A 65-year-old woman is evaluated for worsening urinary urgency and incontinence. The patient has had no abdominal pain, dysuria, or changes in urinary frequency. On several occasions, she has urinated involuntarily, which she attributes to an inability to walk quickly to the bathroom. The patient feels unsteady while ambulating and walks slowly with small steps. Her family also reports that she has become forgetful and has difficulty planning and executing various activities that she used to perform regularly. Medical history is notable for hypertension. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Cardiopulmonary, abdominal, and genitourinary examinations show no abnormalities. Neurological examination shows impaired attention and short-term memory. MRI of the brain reveals chronic white matter changes with no infarction, hemorrhage, or mass lesions. There is diffuse ventriculomegaly with no sulcal enlargement. Which of the following is the most likely underlying cause of this patient's urinary incontinence?

A. Cerebellar dysfunction
B. Compression of the reticular formation
C. Impaired basal ganglia signaling
D. Spinal cord damage



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A. Cerebellar dysfunction
B. Compression of the reticular formation
C. Impaired basal ganglia signaling
D. Spinal cord damage
E. Stretching of descending cortical fibers

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and has difficulty planning and executing various activities that she used to perform regularly. Medical history is notable for hypertension. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Cardiopulmonary, abdominal, and genitourinary examinations show no abnormalities. Neurological examination shows impaired attention and short-term memory. MRI of the brain reveals chronic white matter changes with no infarction, hemorrhage, or mass lesions. There is diffuse ventriculomegaly with no sulcal enlargement. Which of the following is the most likely underlying cause of this patient's urinary incontinence?

A. Cerebellar dysfunction (4%)

B. Compression of the reticular formation (14%)

C. Impaired basal ganglia signaling (15%)

D. Spinal cord damage (4%)

E. Stretching of descending cortical fibers (59%)

Correct

59%

01 min, 13 secs

03/20/2021



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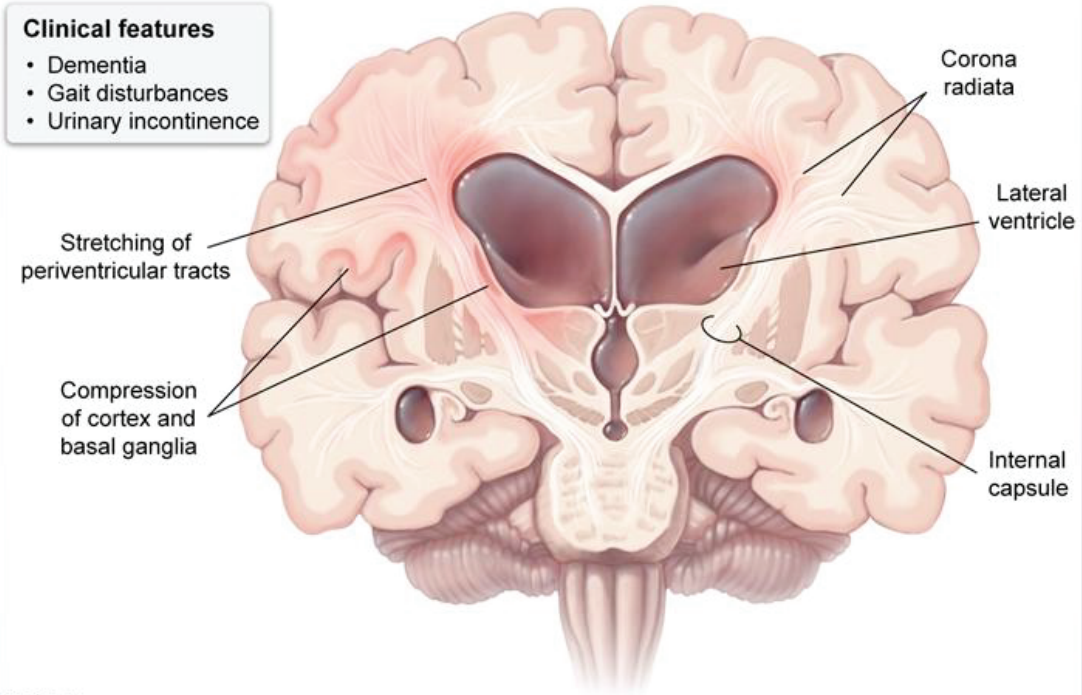
## Normal pressure hydrocephalus

**Clinical features**
- Dementia
- Gait disturbances
- Urinary incontinence

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This patient with impaired memory and cognition, unsteady gait, and urinary incontinence has ventriculomegaly without sulcal enlargement on MRI, which is characteristic of **normal pressure hydrocephalus (NPH)**. NPH can occur due to decreased absorption of cerebrospinal fluid (CSF) by the arachnoid granulations (eg, fibrosis from previous cerebral inflammation or bleeding) with gradual accumulation of CSF in the ventricular system. The lateral ventricles expand, resulting in normal intracranial pressure and **stretching the descending cortical fibers** (corona radiata). Interruption of these pathways, along with impairment of cortical and subcortical function, leads to the classic triad of NPH symptoms (**dementia**, **gait disturbance**, **urinary incontinence**).

The cerebral cortex (through the pontine micturition center) regulates the micturition reflex, which is an autonomic spinal reflex mediated by the neurons in the sacral spinal cord. In NPH, the **lack of cortical inhibition** results in **detrusor muscle hyperactivity**. This leads to urinary urgency, which can be worsened by gait abnormalities that limit a patient's ability to quickly get to a bathroom (**urge incontinence**). Progressive frontal lobe impairment leads to the inability to recognize urinary urge, uncontrolled urination, and a lack of concern as the disease progresses.

**(Choice A)** Cerebellar dysfunction can cause an ataxic gait, dysarthria, and intention tremors. Memory dysfunction and urinary incontinence are more indicative of cerebral impairment. NPH typically spares


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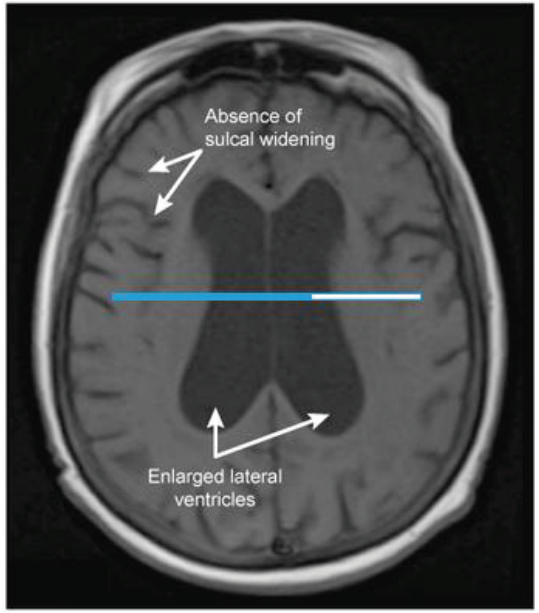
Normal pressure hydrocephalus (NPH)

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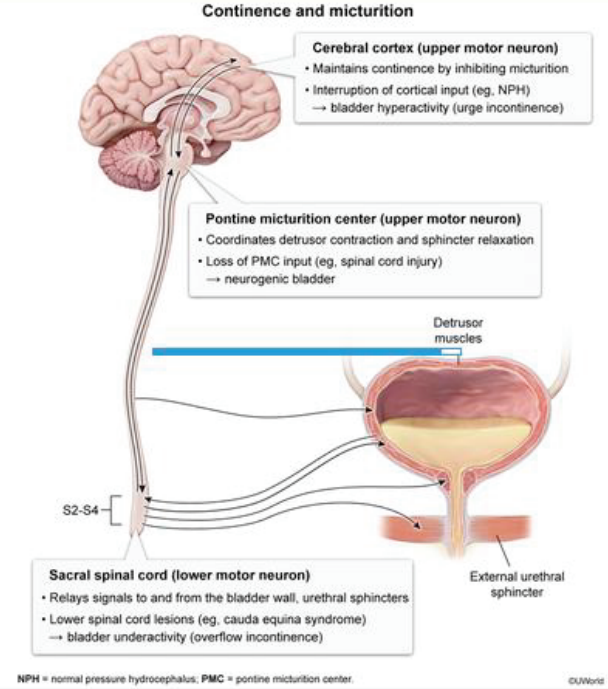


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**(Choice A)** Cerebellar dysfunction can cause an ataxic gait, dysarthria, and intention tremors. Memory dysfunction and urinary incontinence are more indicative of cerebral impairment. NPH typically spares cerebellar function.

**(Choice B)** Compression of the reticular formation can occur with brainstem herniation, leading to loss of consciousness and coma.

**(Choice C)** Impaired basal ganglia signaling is characteristic of Parkinson disease, which can result in ataxia with a slow gait. However, cogwheel rigidity and resting tremor would be prominent and dementia and urinary incontinence would not be expected until later in the disease course.

**(Choice D)** Spinal cord damage is a common cause of incontinence with gait impairment. However, spinal cord injury also frequently causes lower extremity weakness and is not associated with cognitive impairment.

**Educational objective:**
Normal pressure hydrocephalus occurs due to decreased cerebrospinal fluid absorption, resulting in ventriculomegaly with normal intracranial pressure. This causes stretching of the descending cortical fibers (corona radiata) from the frontal lobe and contributes to the classic triad of symptoms (ie, dementia, gait



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**(Choice B)** Compression of the reticular formation can occur with brainstem herniation, leading to loss of consciousness and coma.

**(Choice C)** Impaired basal ganglia signaling is characteristic of Parkinson disease, which can result in ataxia with a slow gait. However, cogwheel rigidity and resting tremor would be prominent and dementia and urinary incontinence would not be expected until later in the disease course.

**(Choice D)** Spinal cord damage is a common cause of incontinence with gait impairment. However, spinal cord injury also frequently causes lower extremity weakness and is not associated with cognitive impairment.

**Educational objective:**
Normal pressure hydrocephalus occurs due to decreased cerebrospinal fluid absorption, resulting in ventriculomegaly with normal intracranial pressure. This causes stretching of the descending cortical fibers (corona radiata) from the frontal lobe and contributes to the classic triad of symptoms (ie, dementia, gait abnormalities, urinary incontinence). Loss of cortical inhibition of the sacral micturition center leads to urge incontinence.

| Pathology | Nervous System | Normal pressure hydrocephalus |
|---|---|---|
| Subject | System | Topic |



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A 22-year-old woman is brought to the emergency department due to a day of fever, headaches, nausea, vomiting, and myalgias that began suddenly last night. This morning, the patient was lethargic, difficult to arouse, and confused. She is an exchange student who came to the United States 3 months ago, and her medical history is unknown. Temperature is 39.4 C (102.9 F), blood pressure is 100/60 mm Hg, pulse is 112/min, and respirations are 18/min. Physical examination shows nuchal rigidity. Skin examination findings are shown in the image.

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Leukocyte count is elevated, and lumbar puncture with cerebrospinal fluid Gram stain establishes the diagnosis. Which of the following is the primary component of the vaccine that could have prevented this patient's current condition?

A. Capsular polysaccharide
B. Inactivated (killed) organisms
C. Inactivated toxic compounds
D. Live attenuated organisms
E. Virus-like particles

Submit



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Leukocyte count is elevated, and lumbar puncture with cerebrospinal fluid Gram stain establishes the diagnosis. Which of the following is the primary component of the vaccine that could have prevented this patient's current condition?

- A. Capsular polysaccharide (85%)
- B. Inactivated (killed) organisms (5%)
- C. Inactivated toxic compounds (2%)
- D. Live attenuated organisms (5%)
- E. Virus-like particles (0%)

Correct

85%

01 min, 04 secs

10/08/2020



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| Vaccine types | | |
|---|---|---|
| **Live attenuated vaccines** | **Nonlive (toxoid, subunit, conjugate, inactivated) vaccines** | |
| • Polio (oral)*<br>• Measles, mumps, & rubella<br>• Rotavirus<br>• Yellow fever<br>• Varicella, zoster | • Influenza (intramuscular)<br>• Pneumococcus<br>• Diphtheria–tetanus–pertussis<br>• Typhoid<br>• Hepatitis A<br>• Hepatitis B<br>• *Haemophilus influenzae* type b | • Human papillomavirus<br>• Meningococcus<br>• Polio (inactivated) |

*Not available in the United States; advised only for developing countries.


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countries.

This patient's rapid-onset headache, fever, altered mental status, nuchal rigidity, and purpuric rash raise strong suspicion for **meningococcal meningitis**. *Neisseria meningitidis* is a gram-negative diplococcus transmitted via aerosolized respiratory droplets. Close living conditions (eg, college **dormitories**, prisons, military barracks) promote its spread. *N meningitidis* has several virulence factors, including a polysaccharide capsule (impairs phagocytosis of the bacteria), lipo-oligosaccharide (induces cytokine production, leading to circulatory collapse), pili (permit bacterial attachment to the respiratory mucosa), and IgA protease (cleaves secretory IgA that would otherwise inactivate the pili). Antibodies against the **polysaccharide capsule** confer immunity to *N meningitidis*.

The meningococcal **vaccines** available in the United States are as follows:

- **Quadrivalent conjugate vaccine: Capsular polysaccharide antigens** (serogroups A, C, Y, and W) are fused to a diphtheroid toxin carrier, which allows the polysaccharides to be displayed on the major histocompatibility complex of antigen-presenting cells. This results in the stimulation of T-cells and provides a stronger, more lasting immunologic response.
- **Serogroup B vaccine:** Capsular polysaccharides from serogroup B are very similar to human neural cell adhesion molecules. This molecular mimicry prevented a polysaccharide vaccine due to difficulty


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- **Serogroup B vaccine:** Capsular polysaccharides from serogroup B are very similar to human neural cell adhesion molecules. This molecular mimicry prevented a polysaccharide vaccine due to difficulty in generating an immune response without increasing the risk of autoimmunity. A vaccine against this serogroup is now available that uses recombinant proteins instead of capsular polysaccharides.

In the United States, the quadrivalent vaccine is part of routine immunizations; the serogroup B vaccine is recommended for specific high-risk populations (eg, those with asplenia or complement deficiency).

**(Choice B)** The influenza vaccination typically contains three or four strains of inactivated virus. Although influenza is often associated with rapid-onset malaise, headache, myalgia, and fever, the presence of nuchal rigidity and purpuric skin rash make meningococcemia more likely.

**(Choice C)** The diphtheria toxoid is used as protein carrier in conjugate vaccines because it allows the polysaccharide antigen to be displayed on the major histocompatibility complex of antigen presenting cells. The toxoid is not the primary component of conjugate vaccines.

**(Choice D)** The measles-mumps-rubella vaccination contains live attenuated versions of these viruses. Measles is associated with the 3 C's (coryza, conjunctivitis, cough) and a maculopapular rash, mumps is associated with salivary gland swelling, and rubella is associated with a diffuse maculopapular rash. A


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**(Choice C)** The diphtheria toxoid is used as protein carrier in conjugate vaccines because it allows the polysaccharide antigen to be displayed on the major histocompatibility complex of antigen presenting cells. The toxoid is not the primary component of conjugate vaccines.

**(Choice D)** The measles-mumps-rubella vaccination contains live attenuated versions of these viruses. Measles is associated with the 3 C's (coryza, conjunctivitis, cough) and a maculopapular rash, mumps is associated with salivary gland swelling, and rubella is associated with a diffuse maculopapular rash. A purpuric rash and nuchal rigidity would be atypical.

**(Choice E)** Virus-like particles are multiprotein structures that illicit a strong B- and T-cell response but contain no viral genetic material, so they are not infectious. Virus-like particles are used in the hepatitis B and human papillomavirus vaccines.

**Educational objective:**

Antibodies against the polysaccharide capsule of *Neisseria meningitidis* provide immunity against this pathogen. Quadrivalent meningococcal vaccines contain capsular polysaccharides from major serotypes (A, C, Y, and W) of *N meningitidis*. Serotype B vaccinations use recombinant proteins.

**References**

- Meningococcal vaccinations.



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www.ncbi.nlm.nih.gov/pubmed/27086142

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- Meningococcal vaccinations.



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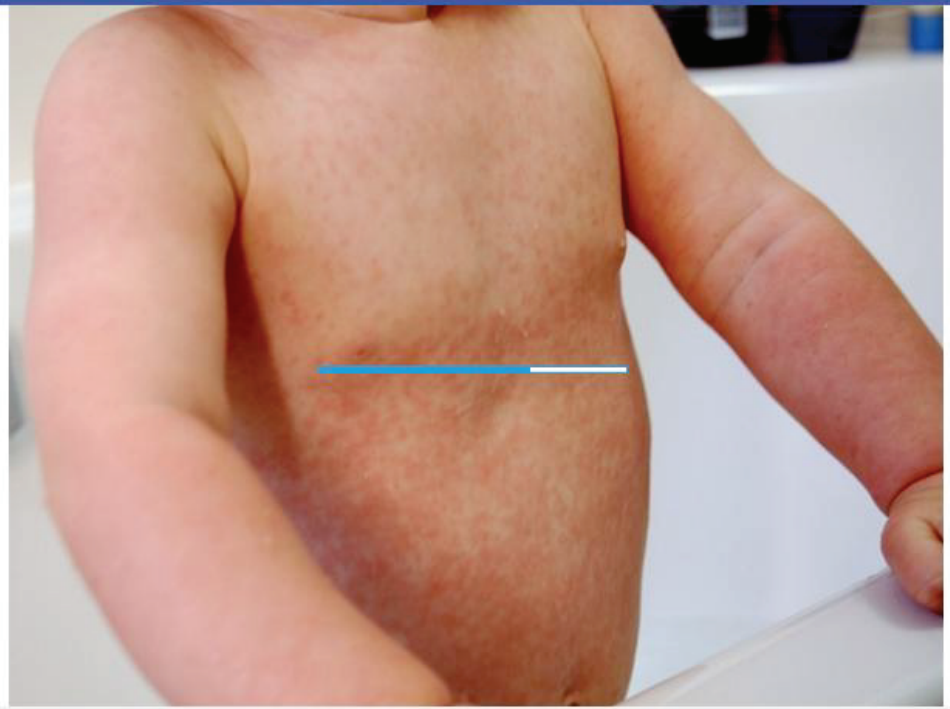

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• Meningococcal vaccinations.



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A 62-year-old man comes to the emergency department due to right upper extremity weakness. Thirty minutes ago, the patient was at his office when he developed difficulty holding a pen. His grip in the right hand was weak and he could not lift his right arm. He tried calling his coworker but could not speak. The patient has never had similar symptoms before. He had no loss of consciousness, weakness of other extremities, vision abnormality, or headache. The symptoms resolved spontaneously by the time paramedics arrived. Medical history is significant for hypertension and a 30-pack-year smoking history. The patient is a defense attorney and recently took on a high-profile case. Temperature is 36.9 C (98.4 F), blood pressure is 140/84 mm Hg, pulse is 82/min and regular, and respirations are 14/min. Physical examination shows no extremity weakness or sensory loss. There is a left carotid bruit; the remainder of the examination shows no abnormalities. Noncontrast CT scan of the head is normal. Which of the following pharmacotherapies is most appropriate in management of this patient?

A. CNS-targeted immunomodulator
B. GABA A receptor modulator
C. HMG-CoA reductase inhibitor
D. Selective serotonin reuptake inhibitor



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A. CNS-targeted immunomodulator
B. GABA A receptor modulator
C. HMG-CoA reductase inhibitor
D. Selective serotonin reuptake inhibitor
E. Tissue plasminogen activator

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extremities, vision abnormality, or headache. The symptoms resolved spontaneously by the time paramedics arrived. Medical history is significant for hypertension and a 30-pack-year smoking history. The patient is a defense attorney and recently took on a high-profile case. Temperature is 36.9 C (98.4 F), blood pressure is 140/84 mm Hg, pulse is 82/min and regular, and respirations are 14/min. Physical examination shows no extremity weakness or sensory loss. There is a left carotid bruit; the remainder of the examination shows no abnormalities. Noncontrast CT scan of the head is normal. Which of the following pharmacotherapies is most appropriate in management of this patient?

A. CNS-targeted immunomodulator (1%)

B. GABA A receptor modulator (4%)

✓ C. HMG-CoA reductase inhibitor (54%)

D. Selective serotonin reuptake inhibitor (4%)

E. Tissue plasminogen activator (35%)

Correct

54%

01 min, 17 secs

03/08/2021



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This patient with cardiovascular risk factors (ie, hypertension, smoking) and a carotid bruit developed right upper extremity weakness and aphasia that resolved without intervention; this is characteristic of a **transient ischemic attack** (TIA), which, in this case, likely occured following atheroembolization or low flow from the patient's carotid artery lesion. TIAs are defined as **focal neurologic deficits** that occur due to **transient brain ischemia**; tissue infarction does not occur, and brain imaging is normal. Symptoms are typically localized to a singular vascular territory and resolve without intervention, typically in <24 hours.

Patients with TIA are at markedly increased risk of future stroke; therefore, intensive medical management is indicated. Secondary prevention includes **antiplatelet agents** (eg, aspirin, clopidogrel) to prevent thrombus formation and **statin** therapy (**HMG-CoA reductase inhibitor**; eg, atorvastatin, rosuvastatin) to reduce atherosclerotic plaque formation. Lifestyle modifications (eg, exercise, tobacco cessation) are also recommended.

**(Choice A)** CNS-targeted immunomodulators (eg, ocrelizumab) or glucocorticoids are used in the treatment of multiple sclerosis (MS), a demyelinating disease that causes relapsing and remitting neurologic deficits. However, MS typically occurs in young women and neurologic deficits are slowly progressive over the course of days.

**(Choice B)** Benzodiazepines (GABA A receptor modulators) are used for acute seizure termination.


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**(Choice B)** Benzodiazepines (GABA A receptor modulators) are used for acute seizure termination. Seizures can cause postictal paralysis but are typically preceded by stereotyped positive symptoms (eg, repetitive limb movement, lip smacking), whereas TIAs often typically cause negative symptoms (eg, loss of limb function, aphasia). In addition, seizure patients often have postictal confusion or sedation.

**(Choice D)** Selective serotonin reuptake inhibitors are used for treating anxiety or depression.

**(Choice E)** Tissue plasminogen activator ([TPA]; eg, alteplase) is used for thrombolysis in patients with acute, potentially debilitating, ischemic stroke, which would present with persistent neurologic deficits. TPA is not indicated as this patient's symptoms resolved without intervention.

**Educational objective:**
Transient ischemic attacks (TIAs) are transient episodes of focal neurologic impairment that occur due to local brain ischemia; tissue infarction does not occur, and brain imaging is normal. Patients with TIA are at increased risk of future stroke; secondary prevention includes antiplatelet agents (eg, aspirin, clopidogrel), statins, and lifestyle modifications (eg, tobacco cessation, exercise) to reduce future risk.

| Pharmacology | Nervous System | Transient ischemic attack |
|---|---|---|
| Subject | System | Topic |

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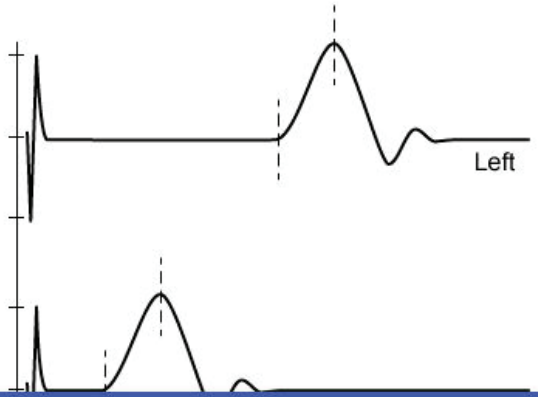
A 38-year-old woman is being evaluated for intermittent tingling and numbness of the left hand for the past several months. Her symptoms predominantly involve the fourth and fifth digits and are often brought on by driving a car. Physical examination shows no abnormalities. An electrodiagnostic study is performed, during which a nerve stimulator is placed on the left fifth digit and a surface recorder is placed over the ulnar nerve above the elbow. Electrical stimulus is applied, and the graph obtained is shown below. Results from the asymptomatic contralateral extremity are also shown. Which of the following is primarily affected in this patient?





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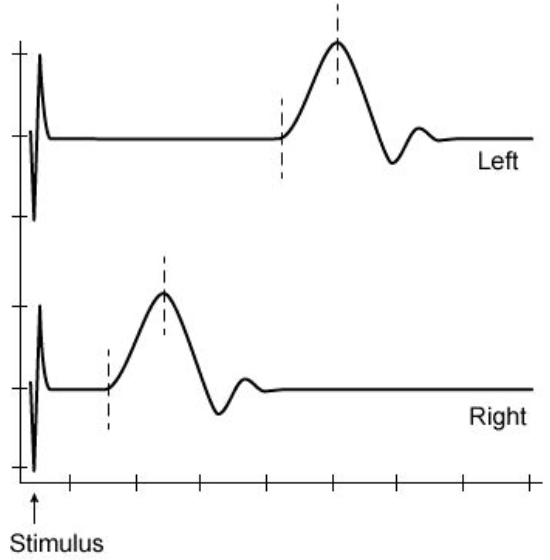


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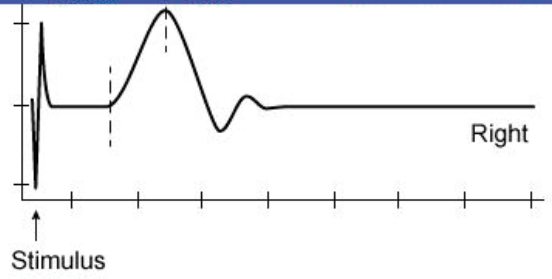


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A. Neuronal axons
B. Neuronal cell bodies
C. Postsynaptic membrane
D. Schwann cells
E. Synaptic vesicles

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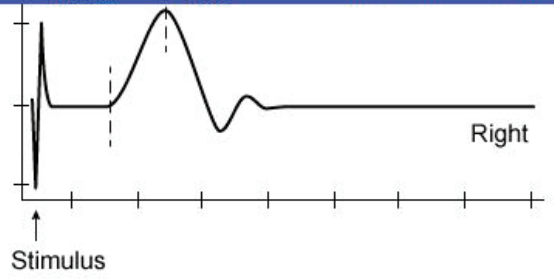


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A. Neuronal axons (23%)

B. Neuronal cell bodies (2%)

C. Postsynaptic membrane (3%)

D. Schwann cells (68%)

E. Synaptic vesicles (1%)

Correct

68%

49 secs

09/23/2020



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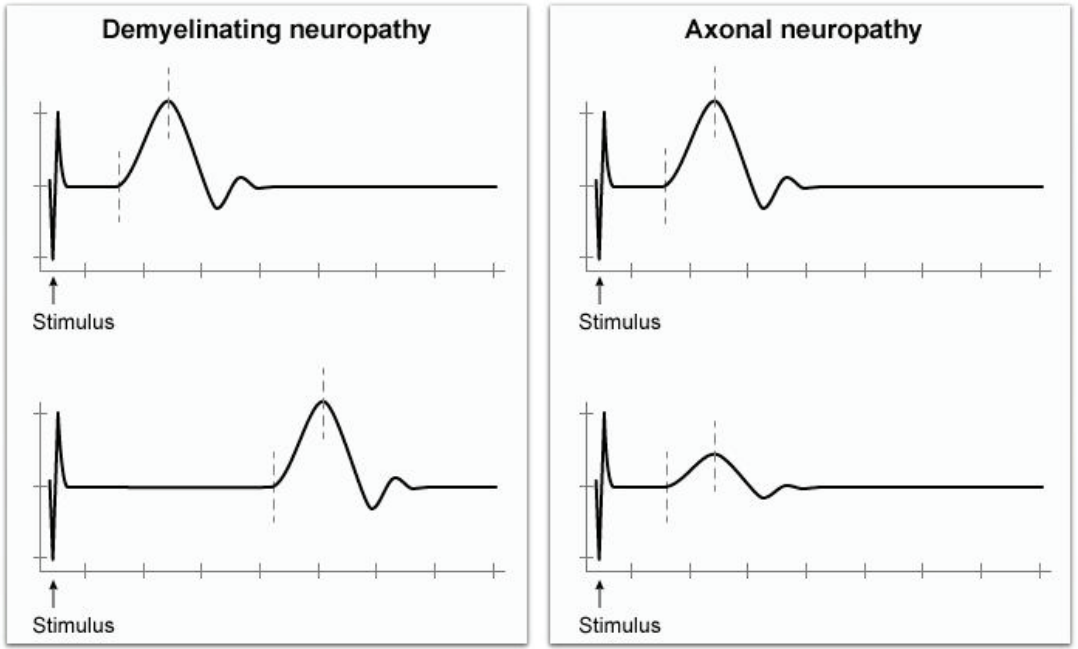


A **nerve conduction study** (NCS) measures the amplitude, velocity, and latency of an electrical stimulus applied to an isolated nerve and can help differentiate between demyelinating and axonal neuropathies:


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A **nerve conduction study** (NCS) measures the amplitude, velocity, and latency of an electrical stimulus applied to an isolated nerve and can help differentiate between demyelinating and axonal neuropathies:

- **Demyelinating neuropathies** are caused by damage to the myelin sheath. Loss of insulation results in **delayed** (or blocked) **nerve conduction velocity**.
- **Axonal neuropathies** are caused by damage to the nerve axon. Loss of axon fibers results in **reduced signal amplitude**.

This patient has a delay in left-sided ulnar conduction velocity, indicating a **demyelinating ulnar mononeuropathy**. Focal nerve **compression** (eg, compression of the ulnar nerve at the elbow) is the most common cause of mononeuropathy and results in nerve ischemia, leading to apoptosis of Schwann cells and **localized demyelination**. In addition to sensory symptoms, patients with ulnar neuropathy may also have weakness of the fourth and fifth digits, elbow pain, and worsening of symptoms with elbow or wrist flexion. Severe disease can lead to wasting of the hand muscles and an ulnar claw deformity.

**(Choice A)** An axonal neuropathy would primarily show diminished amplitude, rather than reduced velocity of nerve conduction. Common causes of axonal neuropathy include diabetes mellitus, toxins (eg, chemotherapeutic drugs), hypothyroidism, vitamin $B_{12}$ deficiency, and vasculitis.



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## Exhibit Display

**Classic hand poses in radial, median, & ulnar nerve lesions**

Sensory loss
Atrophy

Ulnar claw (ulnar palsy)

Preacher's hand (median palsy)

Simian hand (median & ulnar palsy)

Wrist drop (radial palsy)

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**(Choice A)** An axonal neuropathy would primarily show diminished amplitude, rather than reduced velocity of nerve conduction. Common causes of axonal neuropathy include diabetes mellitus, toxins (eg, chemotherapeutic drugs), hypothyroidism, vitamin $B_{12}$ deficiency, and vasculitis.

**(Choice B)** Neuronal cell bodies are located in the dorsal root ganglia and the anterior horn of the spinal cord. Neuronal cell body damage could potentially result in reduced signal amplitude if there is secondary axonal degeneration.

**(Choice C)** Myasthenia gravis is due to autoimmune attack on the acetylcholine receptors of the postsynaptic membrane. This causes fatigable weakness of the ocular, facial, and proximal muscles. NCS is typically normal, but muscle stimulation studies demonstrate a reduction in *motor signal strength* with repetitive stimuli.

**(Choice E)** Botulinum toxin blocks acetylcholine release from presynaptic membranes of the neuromuscular junction by impairing fusion of secretory vesicles with the synaptic membrane. Patients typically develop cranial neuropathies with symmetric, descending flaccid paralysis. NCS is typically normal; muscle stimulation studies may show a reduction in *motor signal strength* that improves with repetitive stimuli.

**Educational objective:**



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is typically normal, but muscle stimulation studies demonstrate a reduction in *motor signal strength* with repetitive stimuli.

**(Choice E)** Botulinum toxin blocks acetylcholine release from presynaptic membranes of the neuromuscular junction by impairing fusion of secretory vesicles with the synaptic membrane. Patients typically develop cranial neuropathies with symmetric, descending flaccid paralysis. NCS is typically normal; muscle stimulation studies may show a reduction in *motor signal strength* that improves with repetitive stimuli.

**Educational objective:**

Ulnar neuropathy is characterized by numbness of the fourth and fifth digits, pain, and weakness. It is most commonly caused by compressive injury, leading to tissue ischemia and demyelination (Schwann cell injury). A nerve conduction study can help differentiate demyelinating versus axonal neuropathies; demyelination causes slowed or blocked nerve conduction velocity whereas axonal injury leads to a reduction in signal strength.

| Pathophysiology | Nervous System | Peripheral neuropathy |
|---|---|---|
| Subject | System | Topic |

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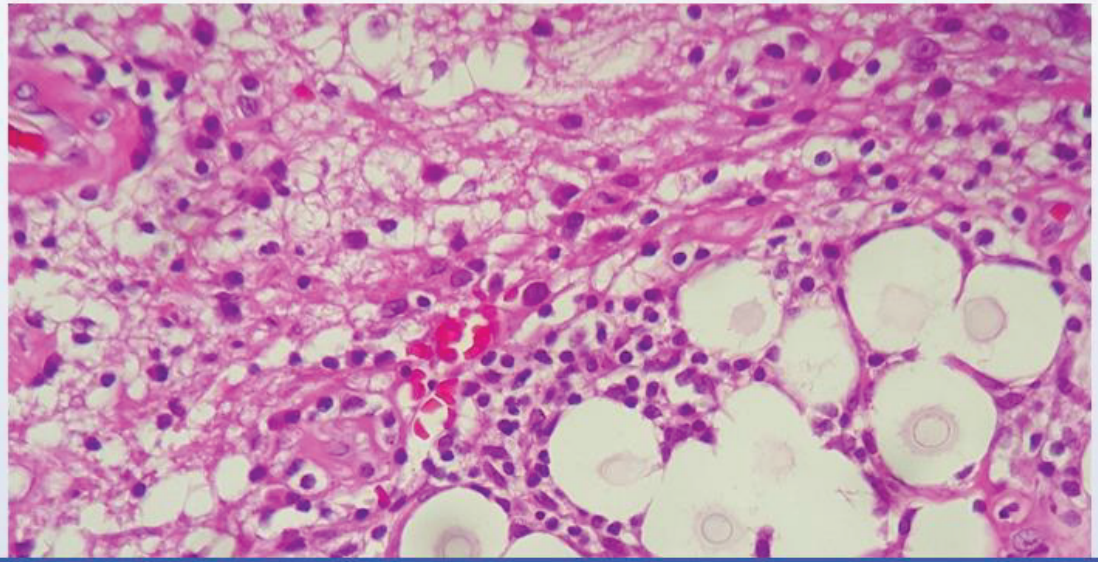
A 38-year-old man is brought to the emergency department after a generalized tonic-clonic seizure. He had several days of progressive headache, vomiting, and confusion prior to the episode. Temperature is 38 C (100.4 F). Physical examination shows a lethargic patient with bilateral papilledema and neck rigidity. His condition progressively worsens, and the patient dies in the hospital several days later. An autopsy is performed, and the brain histopathology is shown below.





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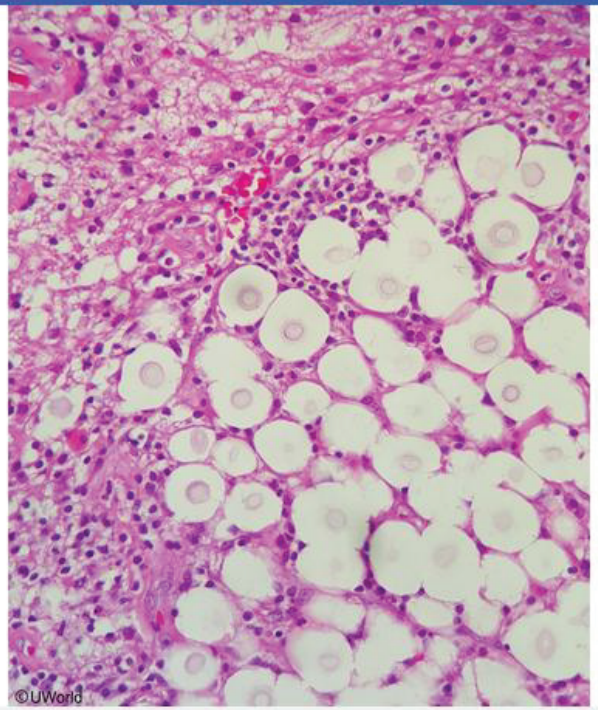


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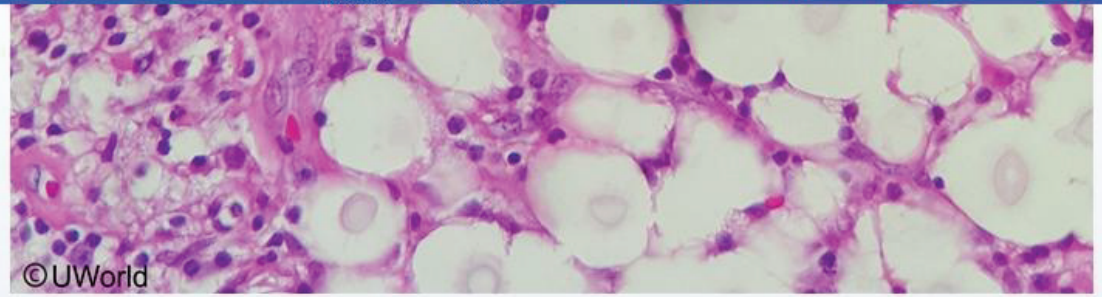


Which of the following pathogens is most likely responsible for these findings?

A. Bacteria with mycolic acid in cell wall
B. Infectious agent lacking nucleic acid
C. Neurotrophic double-stranded DNA virus
D. Obligate intracellular protozoan parasite
E. Yeast with polysaccharide capsule

Submit



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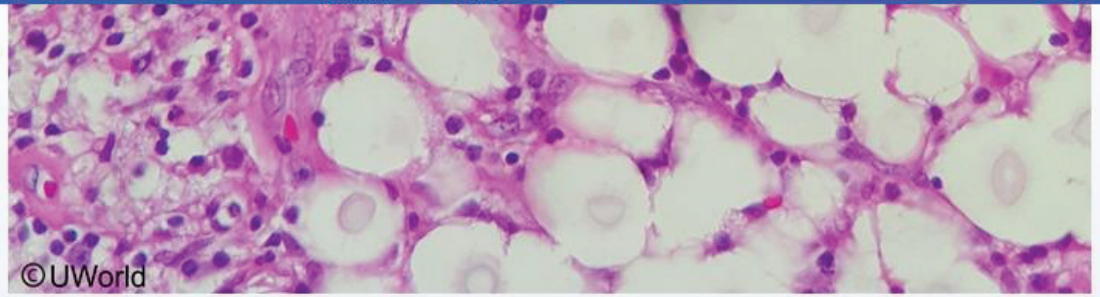


Which of the following pathogens is most likely responsible for these findings?

A. Bacteria with mycolic acid in cell wall (3%)
B. Infectious agent lacking nucleic acid (6%)
C. Neurotrophic double-stranded DNA virus (7%)
D. Obligate intracellular protozoan parasite (13%)
E. Yeast with polysaccharide capsule (68%)

Correct

68%
Answered correctly

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Time Spent

02/06/2021
Last Updated



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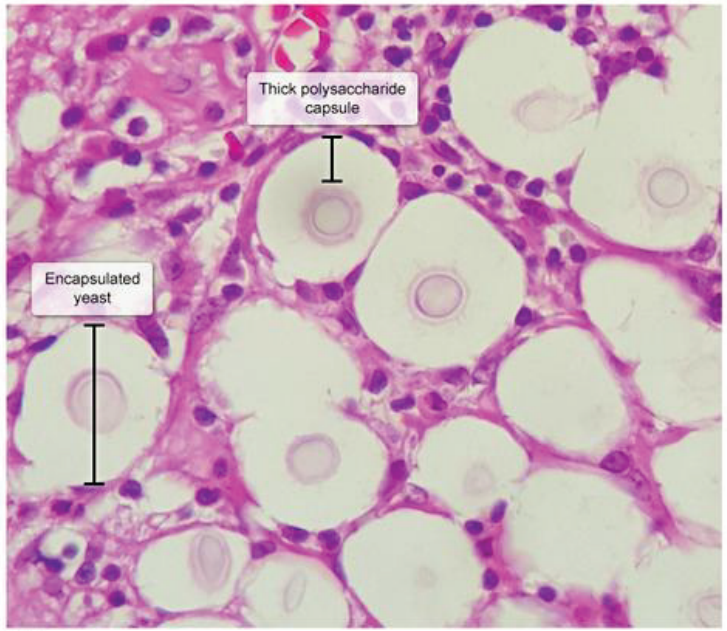
Exhibit Display

Cryptococcal encephalitis

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***Cryptococcus neoformans***, a round/oval yeast surrounded by a **thick polysaccharide capsule** (clear areas on H&E tissue stain shown above), is found primarily in soil contaminated by bird droppings and is transmitted to humans via inhalation. Healthy individuals control/eliminate the infection with the cell-mediated immune response and are rarely symptomatic. However, those with compromised immunity, particularly **advanced AIDS**, cannot contain the infection and often develop hematologic dissemination to the brain (**cryptococcal meningitis**).

Replication of *C neoformans* in the brain clogs the arachnoid villi with yeast antigens and capsular proteins, leading to obstructed cerebrospinal fluid outflow. This **elevates intracranial pressure** and causes slowly progressive headache, nausea and vomiting, confusion, neck rigidity, and papilledema. Seizures and brain herniation can subsequently occur.

The diagnosis is typically confirmed by detection of **cryptococcal antigens** in cerebrospinal fluid (CSF) or visualization of encapsulated, budding yeasts in CSF using specialized stains (eg, India ink, methenamine silver); these special stains are needed as the yeasts are surrounded by clear CSF (unlike in tissue sections). Patients who develop cryptococcal meningitis often are unaware of underlying HIV infection (as is likely in this case); it is considered an AIDS-defining illness.



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**(Choice A)** Mycolic acid is the primary component of the cell wall of *Mycobacterium tuberculosis*. Although pulmonary infection is most common, *M tuberculosis* can spread to the brain and cause subacute meningitis or a focal parenchymal infection called a tuberculoma. Histopathology would show granulomas with giant cells and acid-fast bacteria.

**(Choice B)** Prions, infectious proteins that lack nucleic acid, can cause Creutzfeldt-Jakob disease. Most cases are marked by rapidly progressive dementia and startle myoclonus. Histopathology typically reveals brain atrophy, spongiform vacuoles, and the accumulation of prions in neuronal tissue.

**(Choice C)** Herpes simplex virus is a neurotrophic, double-stranded DNA virus that can spread through the olfactory tract to the olfactory cortex in the temporal lobe of the brain. Patients usually develop acute fever, headache, confusion, and focal neurologic issues. Histopathology typically reveals hemorrhagic inflammation with an infiltration of mononuclear cells.

**(Choice D)** *Toxoplasma gondii* is a feline parasite that can cause encephalitis in patients with untreated AIDS. Manifestations include headache, confusion, fever, seizures, and focal neurologic deficits. However, histopathology would reveal *T gondii* cysts, not encapsulated yeasts.

**Educational objective:**


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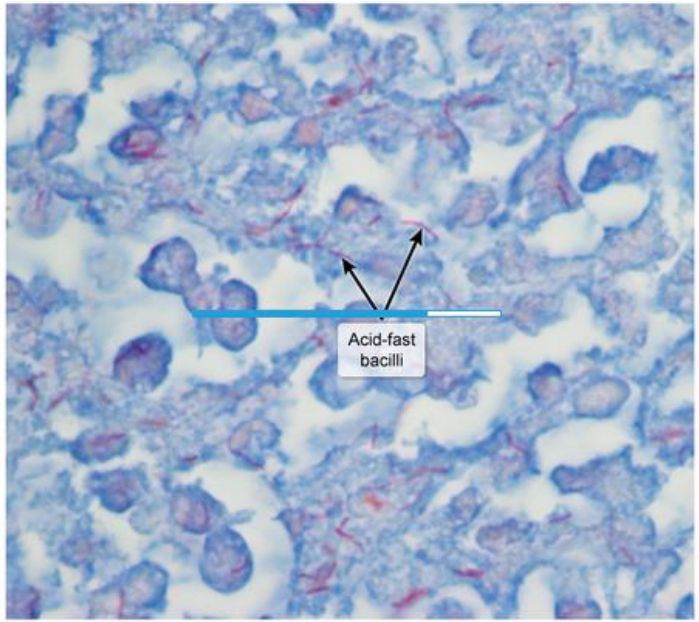
Exhibit Display

Mycobacteria




Acid-fast stain

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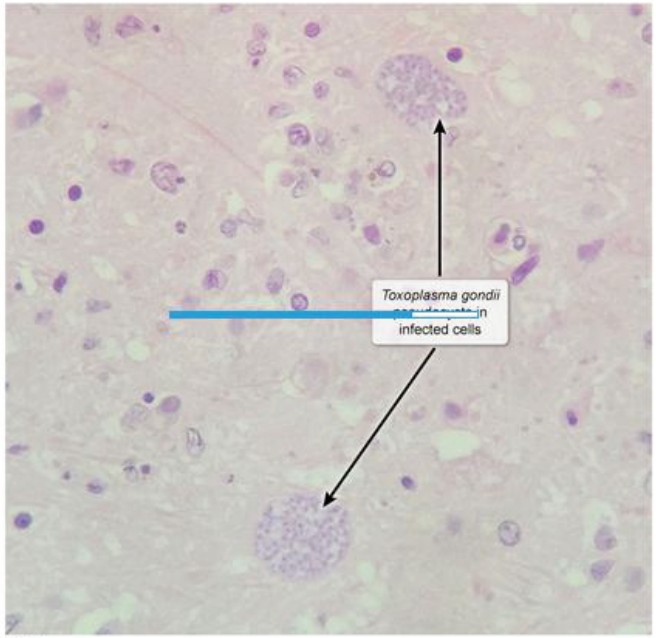
Cerebral toxoplasmosis

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brain atrophy, spongiform vacuoles, and the accumulation of prions in neuronal tissue.

**(Choice C)** Herpes simplex virus is a neurotrophic, double-stranded DNA virus that can spread through the olfactory tract to the olfactory cortex in the temporal lobe of the brain. Patients usually develop acute fever, headache, confusion, and focal neurologic issues. Histopathology typically reveals hemorrhagic inflammation with an infiltration of mononuclear cells.

**(Choice D)** *Toxoplasma gondii* is a feline parasite that can cause encephalitis in patients with untreated AIDS. Manifestations include headache, confusion, fever, seizures, and focal neurologic deficits. However, histopathology would reveal *T gondii* cysts, not encapsulated yeasts.

**Educational objective:**

*Cryptococcus neoformans* is a round/oval yeast with a thick polysaccharide capsule. It is a common cause of meningoencephalitis (eg, headache, vomiting, confusion, seizure) in patients with untreated AIDS. The yeast can frequently be visualized in the cerebrospinal fluid by India ink or silver stain.

| Microbiology | Nervous System | Cryptococcal infections |
|---|---|---|
| Subject | System | Topic |

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A 70-year-old man is brought to the emergency department due to left-sided weakness and slurred speech upon awakening 30 minutes ago. The patient was asymptomatic when he went to bed last night. Medical history includes type 2 diabetes mellitus, hypertension, and hyperlipidemia. The patient is a former smoker with a 30-pack-year history. Physical examination shows a right gaze preference, left lower facial droop, and hemiplegia and hemisensory loss on the left. CT scan of the brain reveals early infarction in the right middle cerebral artery territory with no acute hemorrhage. The patient is hospitalized for further management. Several hours later, he becomes progressively obtunded with elevated intracranial pressure. A repeat CT scan reveals edema in the region of acute infarction causing mass effect. Which of the following is the primary contributor to the pathogenesis of this patient's raised intracranial pressure?

A. Decrease in plasma oncotic pressure
B. Failure of ATP-dependent ion transporters
C. Inadequate absorption of cerebrospinal fluid
D. Increase in capillary hydrostatic pressure
E. Proliferation of astrocytes and microglia


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history includes type 2 diabetes mellitus, hypertension, and hyperlipidemia. The patient is a former smoker with a 30-pack-year history. Physical examination shows a right gaze preference, left lower facial droop, and hemiplegia and hemisensory loss on the left. CT scan of the brain reveals early infarction in the right middle cerebral artery territory with no acute hemorrhage. The patient is hospitalized for further management. Several hours later, he becomes progressively obtunded with elevated intracranial pressure. A repeat CT scan reveals edema in the region of acute infarction causing mass effect. Which of the following is the primary contributor to the pathogenesis of this patient's raised intracranial pressure?

A. Decrease in plasma oncotic pressure (3%)
B. Failure of ATP-dependent ion transporters (46%)
C. Inadequate absorption of cerebrospinal fluid (15%)
D. Increase in capillary hydrostatic pressure (28%)
E. Proliferation of astrocytes and microglia (5%)

Correct
46%
04 mins
10/05/2020


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This patient had a right hemispheric **ischemic stroke** and developed altered mental status and increased intracranial pressure (ICP) secondary to **cerebral edema**. The fixed volume of the skull necessitates that a significant increase in volume of any component of the CNS (eg, brain tissue, blood, cerebrospinal fluid) will raise ICP. This increased ICP can cause progressive **neurologic impairment** through direct pressure-induced cell injury or mechanical damage due to brain herniation.

Irreversible ischemic neural and glial cell injury initiates a sequence of chemical changes that promote edema:

- **Cytotoxic (ionic) edema** begins hours after the ischemic injury due to decreased ATP. The failure of **ATP-dependent ion pumps**, combined with the release of excitatory amino acids (eg, glutamate), leads to the accumulation of intracellular $Na^+$ and water in neural and glial cells despite an intact blood-brain barrier.
- **Vasogenic edema** follows 24-48 hours later, when the release of inflammatory mediators disrupts the tight junctions of the blood-brain barrier, allowing proteins (eg, albumin) and water to enter the interstitial space. This vasogenic phase can cause persistent cerebral edema for weeks after the initial injury.

**(Choice A)** Although a decrease in oncotic pressure can cause peripheral edema (eg, nephrotic


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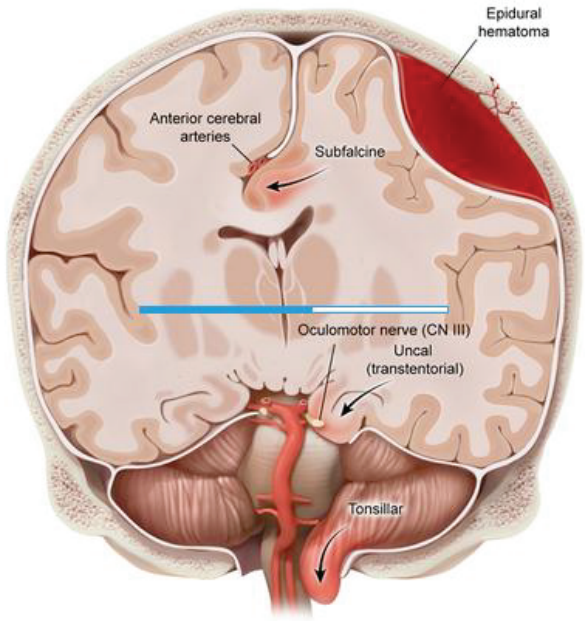
Types of brain herniation

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(Choice A) Although a decrease in oncotic pressure can cause peripheral edema (eg, nephrotic



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**(Choice A)** Although a decrease in oncotic pressure can cause peripheral edema (eg, nephrotic syndrome), it is not a significant factor in the development of cerebral edema. Mannitol is used in the treatment of cerebral edema because it increases plasma oncotic pressure and temporarily disrupts the blood-brain barrier, allowing movement of fluid out of the CNS to decrease ICP.

**(Choice C)** Inadequate absorption of cerebrospinal fluid at the arachnoid granulations can cause communicating hydrocephalus. Although this process raises ICP, ventriculomegaly would likely be prominent on CT scan.

**(Choice D)** Increased hydrostatic pressure secondary to central venous thrombosis or hypertensive encephalopathy can cause cerebral edema and increased ICP. However, patients typically have gradually worsening headache before development of neurologic abnormalities.

**(Choice E)** Gliosis is the process of repairing damaged tissue in the CNS by proliferating astrocytes and microglia. This process occurs slowly in the months to years after CNS injury and would not be expected to cause acute changes in ICP.

**Educational objective:**

The primary mechanism underlying cytotoxic (early) edema following cerebral ischemia is the accumulation of intracellular $Na^+$ and water due to the failure of ATP-dependent ion transporters in hypoxic cells.


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prominent on CT scan.

**(Choice D)** Increased hydrostatic pressure secondary to central venous thrombosis or hypertensive encephalopathy can cause cerebral edema and increased ICP. However, patients typically have gradually worsening headache before development of neurologic abnormalities.

**(Choice E)** Gliosis is the process of repairing damaged tissue in the CNS by proliferating astrocytes and microglia. This process occurs slowly in the months to years after CNS injury and would not be expected to cause acute changes in ICP.

**Educational objective:**

The primary mechanism underlying cytotoxic (early) edema following cerebral ischemia is the accumulation of intracellular $Na^+$ and water due to the failure of ATP-dependent ion transporters in hypoxic cells. Cerebral edema causes progressive neurologic decline by raising intracranial pressure, which can directly damage neural tissue or result in mechanical damage due to brain herniation.

**References**

- Brain edema after ischaemic stroke.

Pathology Nervous System Ischemic stroke



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A 16-year-old boy is evaluated for progressive gait instability, dysmetria, and dysarthria for the past several years. The patient enjoys basketball but can no longer play due to his worsening symptoms. He is worried as his brother died of a neurologic disease at age 21. Physical examination of the lower extremities reveals bilateral motor weakness and loss of deep tendon reflexes, joint position, and vibration sense. MRI of the brain and spine shows degeneration of the posterior columns and spinocerebellar tracts. Which of the following conditions has clinical manifestations that closely resemble this patient's disease?

- A. Acute intermittent porphyria
- B. Lead intoxication
- C. Poliomyelitis
- D. Prion disease
- E. Thiamine deficiency
- F. Vitamin E deficiency

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A 16-year-old boy is evaluated for progressive gait instability, dysmetria, and dysarthria for the past several years. The patient enjoys basketball but can no longer play due to his worsening symptoms. He is worried as his brother died of a neurologic disease at age 21. Physical examination of the lower extremities reveals bilateral motor weakness and loss of deep tendon reflexes, joint position, and vibration sense. MRI of the brain and spine shows degeneration of the posterior columns and spinocerebellar tracts. Which of the following conditions has clinical manifestations that closely resemble this patient's disease?

A. Acute intermittent porphyria (2%)
B. Lead intoxication (6%)
C. Poliomyelitis (28%)
D. Prion disease (3%)
E. Thiamine deficiency (21%)
F. Vitamin E deficiency (36%)


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Vitamin E is a lipid-soluble, antioxidant vitamin that is widely available in the diet. **Vitamin E deficiency** is rare but may occur in patients with fat malabsorption and abetalipoproteinemia. The most notable manifestations include hemolysis and **neurologic dysfunction** (due to free radical damage of cell membranes).

Neurologic symptoms of vitamin E deficiency closely **mimic** Friedreich ataxia (an autosomal recessive degenerative condition) as many of the same areas in the nervous system are affected. Specifically, patients with either condition may have ataxia (due to degeneration of spinocerebellar tracts), loss of position and vibration sense (due to degeneration of the dorsal columns), and loss of deep tendon reflexes (due to peripheral nerve degeneration). Vitamin B12 deficiency may also present similarly due to subacute combined degeneration of the dorsal and lateral spinal columns.

**(Choice A)** Unlike Friedrich ataxia, acute intermittent porphyria does not result in progressive spinal cord degeneration. Instead, it usually causes intermittent acute attacks of abdominal pain and peripheral neuropathy.

**(Choice B)** Lead intoxication is seen in children more often than adults. It manifests with irritability, loss of developmental milestones (in infants), or learning problems (in older children). Gastrointestinal symptoms


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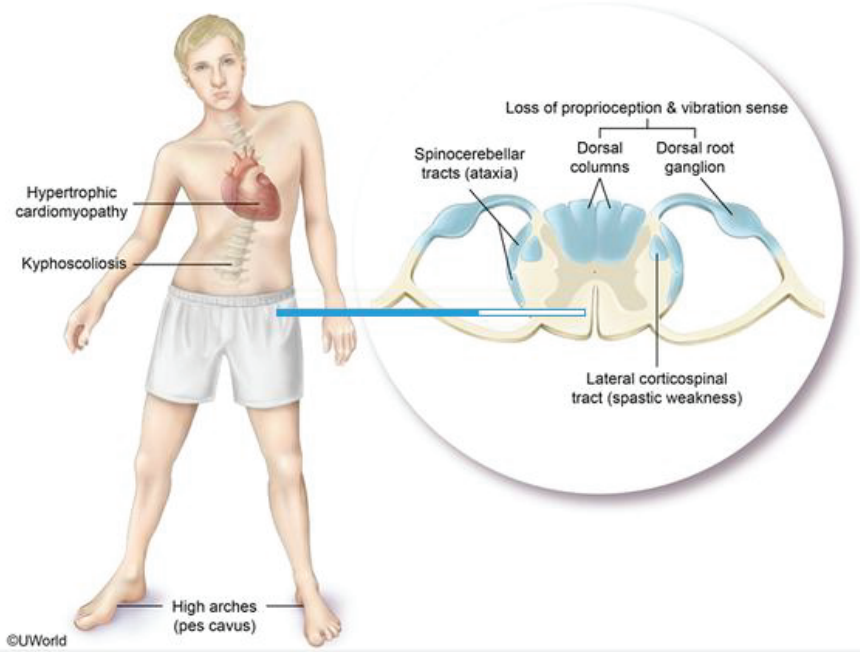
## Friedreich ataxia

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neuropathy.

**(Choice B)** Lead intoxication is seen in children more often than adults. It manifests with irritability, loss of developmental milestones (in infants), or learning problems (in older children). Gastrointestinal symptoms (eg, constipation, nausea, abdominal pain) also occur.

**(Choice C)** Poliomyelitis causes damage to the anterior horn cells and leads to asymmetric flaccid paralysis and hyporeflexia. Sensation is typically preserved.

**(Choice D)** Creutzfeldt-Jakob disease is a prion disease that presents with rapidly progressive dementia and myoclonic jerks of the extremities.

**(Choice E)** Thiamine (vitamin B1) deficiency occurs in alcoholics and malnourished patients. It is associated with peripheral neuropathy, high-output cardiac failure, and Wernicke encephalopathy (eg, ataxia, confusion, ophthalmoplegia).

**Educational objective:**
Vitamin E is a lipid-soluble vitamin that has antioxidative properties. Neurologic symptoms of vitamin E deficiency closely mimic Friedreich ataxia and include ataxia (due to degeneration of spinocerebellar tracts), loss of position and vibration sense (due to degeneration of the dorsal columns), and loss of deep tendon reflexes (due to peripheral nerve degeneration).


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A 64-year-old man comes to the office due to progressive low back pain for the past several months that is beginning to interfere with his job. The patient describes pain in the lower back and buttocks, which worsens with prolonged standing or walking and improves with lying down. He also has occasional sharp, shooting pain that radiates down his right leg. The patient works as a greeter for a local supermarket and was recently given a written warning for taking too many breaks during his shift. He has a history of hypertension and osteoarthritis. Spine imaging reveals degenerative joint changes and a large osteophyte compressing the spinal nerve root exiting through the right neural foramen between the L5 and S1 vertebrae. Which of the following examination findings is most likely present in this patient due to the nerve lesion?

A. Decreased knee reflex
B. Decreased rectal tone
C. Sensory loss in inguinal region
D. Weakness of foot dorsiflexion
E. Weakness of hip flexion



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beginning to interfere with his job. The patient describes pain in the lower back and buttocks, which worsens with prolonged standing or walking and improves with lying down. He also has occasional sharp, shooting pain that radiates down his right leg. The patient works as a greeter for a local supermarket and was recently given a written warning for taking too many breaks during his shift. He has a history of hypertension and osteoarthritis. Spine imaging reveals degenerative joint changes and a large osteophyte compressing the spinal nerve root exiting through the right neural foramen between the L5 and S1 vertebrae. Which of the following examination findings is most likely present in this patient due to the nerve lesion?

A. ~~Decreased knee reflex~~ (7%)
B. Decreased rectal tone (7%)
C. ~~Sensory loss in inguinal region~~ (6%)
✓ D. Weakness of foot dorsiflexion (66%)
E. ~~Weakness of hip flexion~~ (11%)

66%  02 mins, 12 secs  01/14/2021


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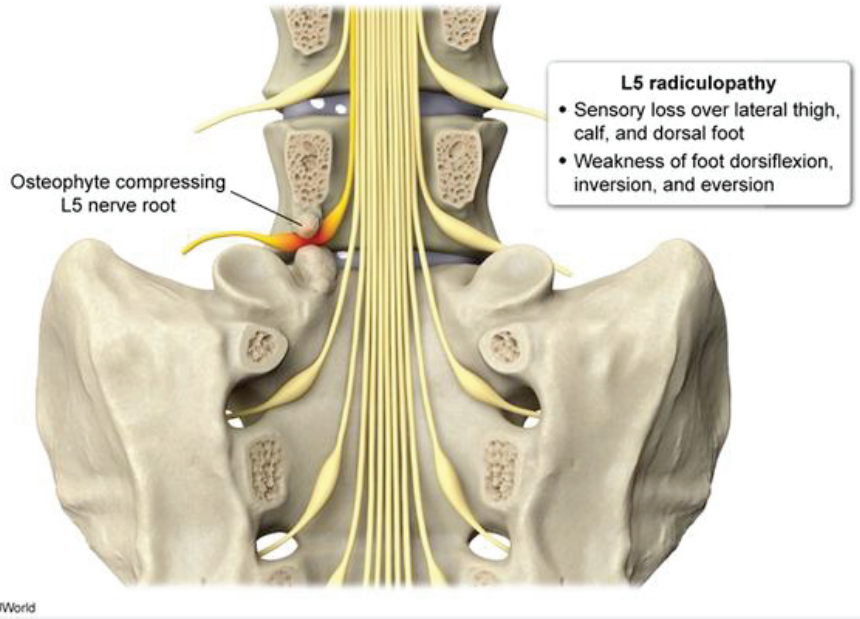
## L5/S1 spondylosis

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This patient has lumbosacral radiculopathy due to an osteophyte at the **L5-S1 neural foramen** resulting in compression of the **L5 nerve root**. Spinal nerves in the lumbosacral spine exit below their corresponding vertebral body level (eg, L5 nerve root exits between L5 and S1 vertebral bodies). However, because of the presence of multiple spinal nerve roots in the lumbosacral area (ie, cauda equina), nerve root compression can occur at different vertebral levels through 2 distinct mechanisms:

- **Spinal spondylosis:** Degenerative changes and osteophyte formation can narrow the neural foramina. This leads to nerve root compression as it **passes through the neural foramina** (in this patient, an osteophyte is compressing the exiting L5 nerve root).
- **Vertebral disc herniation:** A tear in the intervertebral disc annulus can lead to herniation of the nucleus pulposus. If this occurs laterally, it can compress the exiting nerve root as it passes through the neural foramina. However, if it occurs more centrally, it can protrude into the spinal canal and compress other nerves in the cauda equina that exit one or more **levels below the area of herniation**.

L5 radiculopathy causes sensory loss and back pain that radiates down the leg in an L5 dermatomal distribution (eg, buttocks, lateral thigh and calf, dorsal foot). Weakness occurs in muscles innervated by


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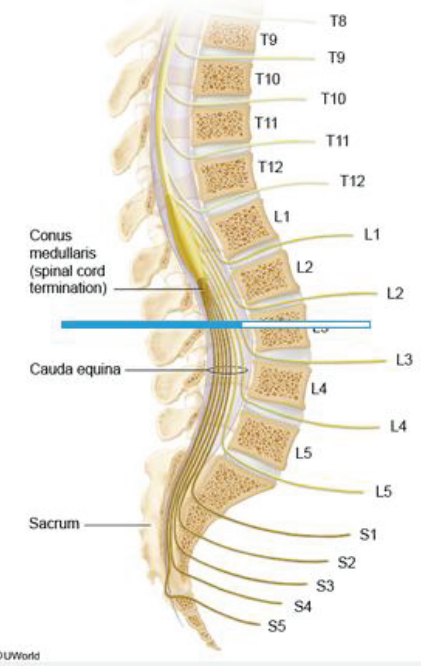
## Exhibit Display

Relation of spinal nerve roots to vertebrae

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distribution (eg, buttocks, lateral thigh and calf, dorsal foot). Weakness occurs in muscles innervated by



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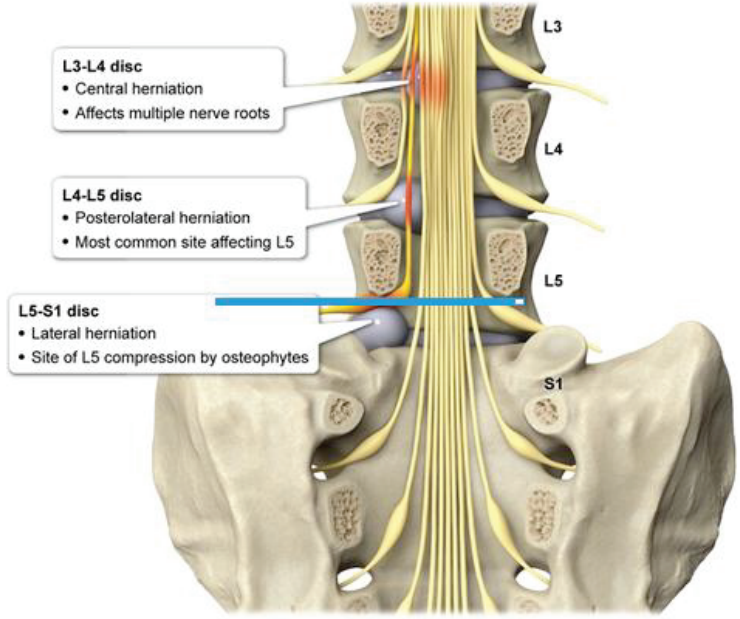
Exhibit Display

L5 radiculopathy

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distribution (eg, buttocks, lateral thigh and calf, dorsal foot). Weakness occurs in muscles innervated by



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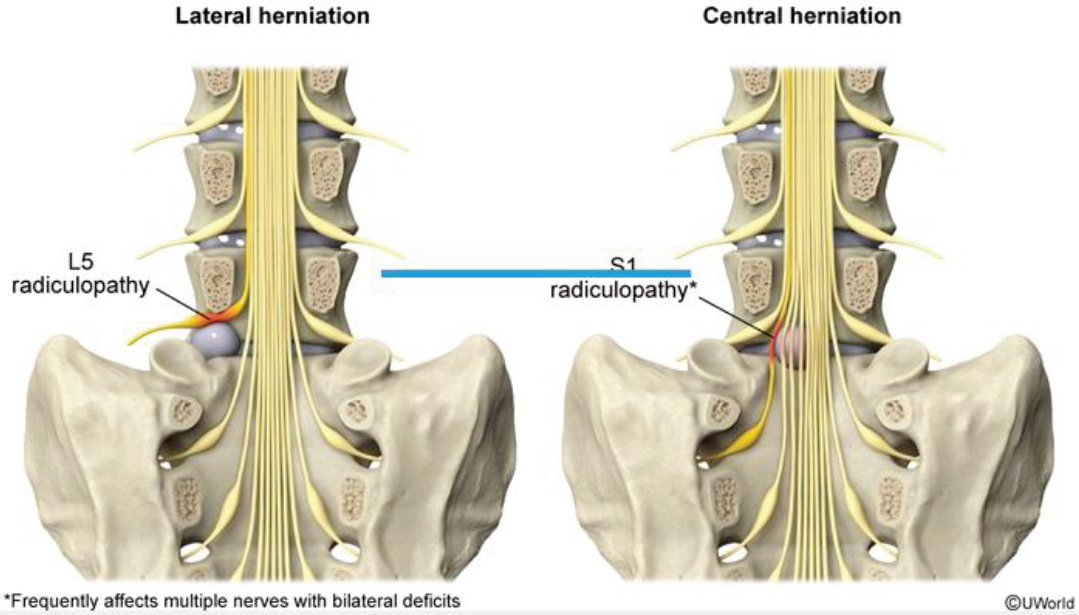
Exhibit Display

## L5/S1 disc herniations

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distribution (eg, buttocks, lateral thigh and calf, dorsal foot). Weakness occurs in muscles innervated by



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**herniation**.

L5 radiculopathy causes sensory loss and back pain that radiates down the leg in an L5 dermatomal distribution (eg, buttocks, lateral thigh and calf, dorsal foot). Weakness occurs in muscles innervated by fibers from the L5 spinal root, which include the tibialis anterior (**foot dorsiflexion** and inversion), peroneus (foot eversion), and extensor hallucis longus (great toe extension).

**(Choice A)** The patellar (knee) reflex is mediated by the quadriceps muscle, which is innervated by L2-L4 nerve roots.

**(Choice B)** Decreased rectal tone can be seen with damage to the pudendal nerve, which originates from the S2-S4 nerve roots.

**(Choice C)** The skin overlying the inguinal region is innervated by fibers from the L1 spinal nerve root that travel in the ilioinguinal and genitofemoral nerves.

**(Choice E)** Hip flexion occurs due to contraction of the iliopsoas, which is innervated by the L2-L4 nerve roots.

**Educational objective:**
Spinal nerves in the lumbosacral spine exit through the neural foramina that is below the corresponding


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herniation.

L5 radiculopathy ca
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**(Choice A)** The pa
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**(Choice E)** Hip fle
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**Educational objec**
Spinal nerves in the

Exhibit Display

**Features of lumbosacral radiculopathy**

| Nerve Root | Reflex affected | Sensory loss* | Weakness |
|---|---|---|---|
| **L2-L4**** | • Patellar | • Anteromedial thigh<br>• Medial shin | • Hip flexion (iliopsoas)<br>• Hip adduction<br>• Knee extension (quadriceps) |
| **L5** | • None | • Lateral shin<br>• Dorsum of the foot | • Foot dorsiflexion & inversion (tibialis anterior)<br>• Foot eversion (peroneus)<br>• Toe extension (extensor hallucis and digitorum) |
| **S1** | • Achilles | • Posterior calf<br>• Sole & lateral foot | • Hip extension (gluteus maximus)<br>• Foot plantarflexion (gastrocnemius) |
| **S2-S4**** | • Anocutaneous | • Perineum | • Urinary or fecal incontinence<br>• Sexual dysfunction |

*Radicular pain typically has a similar distribution to sensory loss.
** Difficult to distinguish between individual nerve roots clinically.

New | Existing



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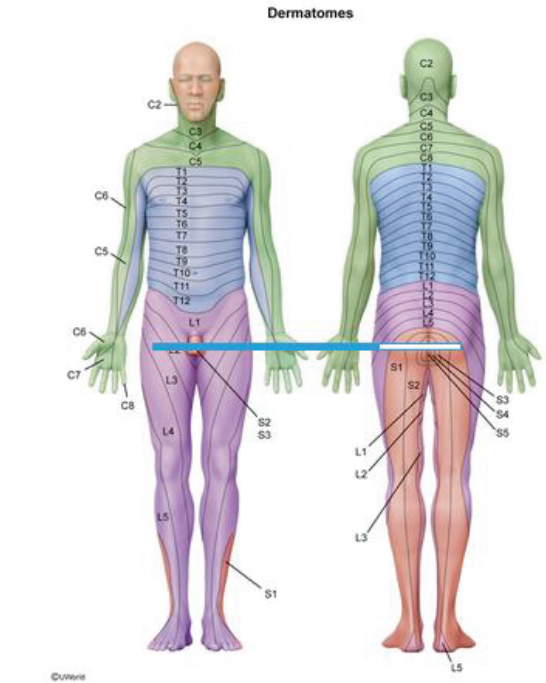


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nerve roots.

**(Choice B)** Decreased rectal tone can be seen with damage to the pudendal nerve, which originates from the S2-S4 nerve roots.

**(Choice C)** The skin overlying the inguinal region is innervated by fibers from the L1 spinal nerve root that travel in the ilioinguinal and genitofemoral nerves.

**(Choice E)** Hip flexion occurs due to contraction of the iliopsoas, which is innervated by the L2-L4 nerve roots.

**Educational objective:**

Spinal nerves in the lumbosacral spine exit through the neural foramina that is below the corresponding vertebral body level (eg, L5 nerve root exits between L5 and S1 vertebral bodies) and can be compressed at the neural foramina due to osteophyte formation. In addition to back pain, L5 radiculopathy often presents with sensory loss over the lateral thigh, calf, and dorsal foot and weakness of great toe extension and foot dorsiflexion, inversion, and eversion.

**References**

- A review of lumbar radiculopathy, diagnosis, and treatment.



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A 40-year-old man comes to the emergency department 30 minutes after experiencing a seizure. Over the past 3 months, the patient has had several episodes of brief twitching of the right hand, but today the abnormal movement gradually progressed to involve the entire right upper extremity, followed by shaking of the whole body for about a minute. He also lost consciousness and urinated involuntarily during the event. The patient feels groggy and has a mild headache. He has no other medical conditions but reports several concussions from playing football in college. Vital signs are within normal limits. Physical examination shows mild weakness of right hand grip but is otherwise normal. This patient's seizure presentation is most suggestive of which of the following etiologic processes?

A. Diffuse cerebral hypoperfusion
B. Focal structural abnormality
C. Genetic epilepsy syndrome
D. Neuroexcitatory substance use
E. Neuronal metabolic disturbance


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past 3 months, the patient has had several episodes of brief twitching of the right hand, but today the abnormal movement gradually progressed to involve the entire right upper extremity, followed by shaking of the whole body for about a minute. He also lost consciousness and urinated involuntarily during the event. The patient feels groggy and has a mild headache. He has no other medical conditions but reports several concussions from playing football in college. Vital signs are within normal limits. Physical examination shows mild weakness of right hand grip but is otherwise normal. This patient's seizure presentation is most suggestive of which of the following etiologic processes?

A. Diffuse cerebral hypoperfusion (10%)
✓ B. Focal structural abnormality (68%)
C. Genetic epilepsy syndrome (2%)
D. Neuroexcitatory substance use (1%)
E. Neuronal metabolic disturbance (16%)

Correct

68%
Answered correctly

01 min, 14 secs
Time Spent

10/05/2020
Last Updated



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This patient with prior episodes of isolated hand twitching (characteristic of focal aware seizures) now experienced a **focal-onset seizure** that progressed to a bilateral tonic-clonic seizure (previously secondarily generalized seizure) with loss of consciousness and involuntary urination.

Focal-onset seizures are caused by a regional area of hypersynchronized **excitatory neural activity** that originates in a **single hemisphere** (in contrast to generalized-onset seizures, which originate globally throughout the cerebral cortex) and are subcategorized by level of consciousness during the event:

- Focal aware seizures (formerly simple partial seizures): Patients remain **aware and interactive**. Symptoms correspond to the area of brain involvement; for example, **twitching/jerking** of the face or limb **(motor cortex of frontal lobe)**, paresthesia (somatosensory cortex of parietal lobe), auditory/olfactory hallucinations (temporal lobe), or visual hallucinations (occipital lobe).
- Focal impaired awareness seizures (formerly complex partial seizures): Patients appear awake but do not interact appropriately with their environment (eg, blank stare). They frequently engage in repetitive, stereotyped actions known as automatisms (eg, lip smacking, hand wringing, repeating words).

The most common underlying cause of focal-onset seizures is a **focal structural brain abnormality** (eg, cerebral neoplasms, stroke, hippocampal sclerosis). These seizures can remain localized or **generalize** to


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Exhibit Display

| Seizure type | Description | Preferred anticonvulsants |
|---|---|---|
| **Focal onset** (involves a single cerebral hemisphere at onset) | | |
| **Aware** | • No loss of consciousness or postictal state<br>• Motor, sensory, autonomic, or cognitive symptoms | • Carbamazepine*<br>• Lamotrigine<br>• Levetiracetam<br>• Phenytoin* |
| **Impaired awareness** | • Appears awake but consciousness is altered (eg, blank stare)<br>• Postictal state<br>• May have automatisms (eg, lip smacking) | |
| **Generalized onset** (involves both hemispheres at onset) | | |
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |
| | • Brief episodes of altered consciousness (eg, blank stare) | • Ethosuxamide |

New | Existing

This patient with pr
experienced a **foca**
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  Symptoms cor
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The most common
cerebral neoplasm



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The most common
cerebral neoplasm

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| | | |
|---|---|---|
| **Aware** | • No loss of consciousness or postictal state<br>• Motor, sensory, autonomic, or cognitive symptoms | • Carbamazepine*<br>• Lamotrigine<br>• Levetiracetam<br>• Phenytoin* |
| **Impaired awareness** | • Appears awake but consciousness is altered (eg, blank stare)<br>• Postictal state<br>• May have automatisms (eg, lip smacking) | |
| **Generalized onset** (involves both hemispheres at onset) | | |
| **Tonic-clonic** | • Loss of consciousness & postictal state<br>• Diffuse muscle contraction of limbs (tonic) followed by rhythmic jerking (clonic) | • Levetiracetam<br>• Valproic acid |
| **Myoclonic** | • No loss of consciousness or postictal state<br>• Brief jerking movements | |
| **Absence** | • Brief episodes of altered consciousness (eg, blank stare)<br>• May have automatisms<br>• Usually no postictal state | • Ethosuximide<br>• Valproic acid |

*Narrow-spectrum agents can also treat focal-onset seizures that evolve into bilateral tonic-clonic seizures.

New | Existing



https://t.me/USMLEWorldStep1

words).

The most common underlying cause of focal-onset seizures is a **focal structural brain abnormality** (eg, cerebral neoplasms, stroke, hippocampal sclerosis). These seizures can remain localized or **generalize** to involve both hemispheres (focal to bilateral tonic-clonic) and are frequently associated with **postictal focal neurologic deficits** (eg, this patient's right hand weakness).

**(Choices A, D, and E)** Diffuse cerebral hypoperfusion, neuroexcitatory substance use, and neuronal metabolic disturbances (except hyperglycemia, which can cause focal seizures) all affect the brain globally and therefore are more likely to present as a generalized seizure rather than a focal seizure. Generalized seizures are characterized by widespread and rapid propagation of neuronal hyperexcitability without the initial localizing symptoms of a focal abnormality.

**(Choice C)** Genetic epilepsy syndromes can have either focal seizures (eg, benign focal epilepsy of infancy) or generalized seizures (eg, Lennox-Gastaut syndrome), but these conditions typically present in childhood and persist into adulthood.

**Educational objective:**
Focal-onset seizures most commonly occur due to a focal structural abnormality (eg, stroke, neoplasm) that causes a region of hyperexcitable neuronal activity in one cerebral hemisphere. These seizures begin


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metabolic disturbances (except hyperglycemia, which can cause focal seizures) all affect the brain globally and therefore are more likely to present as a generalized seizure rather than a focal seizure. Generalized seizures are characterized by widespread and rapid propagation of neuronal hyperexcitability without the initial localizing symptoms of a focal abnormality.

**(Choice C)** Genetic epilepsy syndromes can have either focal seizures (eg, benign focal epilepsy of infancy) or generalized seizures (eg, Lennox-Gastaut syndrome), but these conditions typically present in childhood and persist into adulthood.

**Educational objective:**

Focal-onset seizures most commonly occur due to a focal structural abnormality (eg, stroke, neoplasm) that causes a region of hyperexcitable neuronal activity in one cerebral hemisphere. These seizures begin with localized symptomatology (eg, muscle twitching, paresthesia) and are classified according to level of consciousness (eg, aware, impaired awareness). They can progress to bilateral tonic-clonic seizures if the excitatory neuronal activity spreads to involve both cerebral hemispheres.

| Pathophysiology | Nervous System | Seizures |
|---|---|---|
| Subject | System | Topic |



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A 44-year-old man comes to the office due to paresthesia and pain in his feet. The patient began experiencing tingling and numbness in his toes several months ago, which gradually progressed to the rest of both feet. He has also had burning pain on the soles, which frequently disrupts his sleep at night. The patient has a 6-year history of HIV infection. He was not adherent to treatment initially but now takes antiretroviral therapy regularly. His most recent CD4 cell count was 550/mm$^3$. Vital signs are within normal limits. Foot examination shows decreased pain and touch sensation and loss of ankle reflexes bilaterally. There are no other focal neurologic deficits. Medication review shows no neurotoxic drugs and laboratory studies are within normal limits. Treatment with duloxetine is planned. This medication is most likely to improve this patient's symptoms via which of the following mechanisms?

A. Decreased sensitization of sensory afferent neurons
B. Decreased substance P-induced activation of dorsal horn neurons
C. Frequency-dependent blockade of neuronal conductance
D. Inhibition of GABA release by periaqueductal gray neurons
E. Norepinephrine-mediated descending pain pathway modulation


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of both feet. He has also had burning pain on the soles, which frequently disrupts his sleep at night. The patient has a 6-year history of HIV infection. He was not adherent to treatment initially but now takes antiretroviral therapy regularly. His most recent CD4 cell count was 550/mm$^3$. Vital signs are within normal limits. Foot examination shows decreased pain and touch sensation and loss of ankle reflexes bilaterally. There are no other focal neurologic deficits. Medication review shows no neurotoxic drugs and laboratory studies are within normal limits. Treatment with duloxetine is planned. This medication is most likely to improve this patient's symptoms via which of the following mechanisms?

A. ~~Decreased sensitization of sensory afferent neurons~~ (7%)

B. ~~Decreased substance P-induced activation of dorsal horn neurons~~ (10%)

C. Frequency-dependent blockade of neuronal conductance (4%)

D. ~~Inhibition of GABA release by periaqueductal gray neurons~~ (4%)

✓ E. Norepinephrine-mediated descending pain pathway modulation (72%)

Correct

72%

02 mins, 12 secs

02/03/2021



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| Drugs for neuropathic pain | |
|---|---|
| **Drug** | **Mechanism of action** |
| Tricyclic antidepressants (eg, amitriptyline, nortriptyline)<br><br>SNRIs (eg, duloxetine) | • ↓ Reuptake of serotonin & norepinephrine<br>• Inhibition of pain signals |
| Anticonvulsants (eg, gabapentin, pregabalin) | • Decreased depolarization of neurons in CNS |
| Opioids | • Activation of central opioid receptors |
| Capsaicin (topical) | • Loss of membrane potential in nociceptive fibers |
| Lidocaine (topical) | • Decreased depolarization of neurons in peripheral nerves |

**CNS** = central nervous system; **SNRIs** = serotonin-norepinephrine reuptake inhibitors.

This patient with HIV **peripheral neuropathy** is being treated with **duloxetine**, a serotonin-norepinephrine


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**CNS** = central nervous system; **SNRIs** = serotonin-norepinephrine reuptake inhibitors.

This patient with HIV **peripheral neuropathy** is being treated with **duloxetine**, a serotonin-norepinephrine reuptake inhibitor (SNRI). Because SNRIs increase norepinephrine in the central synapses, they modulate the descending pain pathway, leading to **decreased central perception of pain**.

First-line therapy for painful neuropathy includes the following 3 classes of medications:

- **Tricyclic antidepressants** (eg, nortriptyline, amitriptyline) modulate pain transmission by inhibiting voltage-gated sodium channels in sensory nerves and increasing norepinephrine signaling in the CNS.
- **Serotonin-norepinephrine reuptake inhibitors (SNRIs)** (eg, duloxetine, venlafaxine) alter central transmission of pain by increasing norepinephrine in the central synapses.
- **Anticonvulsants** (eg, gabapentin, pregabalin) inhibit the release of excitatory neurotransmitters by binding to voltage-gated calcium modulators on nerve terminals.

**(Choice A)** Nonsteroidal anti-inflammatory drugs have an analgesic effect that is mediated by decreased sensitization of sensory afferent neurons. They are effective in treating pain due to inflammation but not for neuropathic pain.

**(Choices B and D)** Opioids reduce pain perception at multiple levels. At the spinal level, they lead to


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sensitization of sensory afferent neurons. They are effective in treating pain due to inflammation but not for neuropathic pain.

**(Choices B and D)** Opioids reduce pain perception at multiple levels. At the spinal level, they lead to decreased substance P–induced activation of dorsal horn neurons. At the supraspinal level, they inhibit GABA release by the periaqueductal gray neurons. They are possibly effective for neuropathic pain, but they are not recommended as initial treatment due to the risk of abuse and dependence.

**(Choice C)** Carbamazepine, an anticonvulsant that works by frequency-dependent blockade of neuronal conductance, is used to treat trigeminal neuralgia.

**Educational objective:**
Serotonin-norepinephrine reuptake inhibitors are often used for neuropathic pain. They increase norepinephrine in the central synapses, which modulates the descending pain pathway, leading to decreased central perception of pain.

| Pharmacology | Nervous System | Peripheral neuropathy |
|---|---|---|
| Subject | System | Topic |

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A 56-year-old man is brought to the emergency department due to weakness and difficulty speaking. He has a history of hypertension, cigarette smoking, and polysubstance use. The patient experienced a headache while smoking crack cocaine the previous night. This morning, he was found on the bed unable to move or speak. On physical examination, the patient is awake with normal pupillary responses. Vertical eye movements are intact, but horizontal eye movements are impaired. There is loss of motor strength in the upper and lower extremities bilaterally. Ischemic infarction from cocaine-induced vasospasm is suspected. A lesion involving which of the brain regions is the most likely cause of this patient's current condition?

A. Angular gyrus
B. Cingulate gyrus
C. Ventral midbrain
D. Ventral pons
E. Medial medulla
F. Lateral medulla



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has a history of hypertension, cigarette smoking, and polysubstance use. The patient experienced a headache while smoking crack cocaine the previous night. This morning, he was found on the bed unable to move or speak. On physical examination, the patient is awake with normal pupillary responses. Vertical eye movements are intact, but horizontal eye movements are impaired. There is loss of motor strength in the upper and lower extremities bilaterally. Ischemic infarction from cocaine-induced vasospasm is suspected. A lesion involving which of the brain regions is the most likely cause of this patient's current condition?

- A. ~~Angular gyrus~~ (3%)
- B. ~~Cingulate gyrus~~ (7%)
- C. ~~Ventral midbrain~~ (18%)
- ✓ D. Ventral pons (55%)
- ✗ E. Medial medulla (10%)
- F. ~~Lateral medulla~~ (4%)

Incorrect



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This patient with quadriplegia and speechlessness with preserved consciousness and eye movements has **locked-in syndrome**, which can be caused by ischemic injury to the **bilateral ventral pons**. Locked-in syndrome classically leads to:

- Absent voluntary motor function of the limbs **(quadriplegia)** and oral structures **(loss of speech)** due to destruction of the cortical spinal and cortical bulbar pathways, which prevents cranial nerves or the limbs from receiving cortical signals.
- **Absent horizontal eye movements**. However, vertical eye movements and eyelid elevation are preserved because they are controlled in the rostral midbrain.
- **Preserved consciousness** because the midbrain reticular formation is spared **(Choice C)**. Behavioral arousal and sleep-wake cycles are also preserved because the diencephalon–upper brainstem arousal systems are unaffected.
- **Preserved sensation** because sensory pathways are not affected and preserved brainstem and spinal reflexes because they do not require cortical input.

**(Choice A)** Damage to the angular gyrus of the dominant parietal lobe classically results in Gerstmann


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reflexes because they do not require cortical input.

**(Choice A)** Damage to the angular gyrus of the dominant parietal lobe classically results in Gerstmann syndrome, which is characterized by agraphia (inability to write), acalculia (inability to carry out mathematical calculations), finger agnosia (inability to identify individual fingers on the hand), and left-right disorientation.

**(Choice B)** Damage to the cingulate gyrus can result in significant behavioral symptoms (eg, abulia).

**(Choice E)** Damage to the medial medulla can result in contralateral hemiparesis (due to damage of the lateral corticospinal tract), contralateral hemisensory loss (dorsal column/medial lemniscal pathway), and ipsilateral tongue paralysis (hypoglossal nucleus).

**(Choice F)** Damage to the lateral medulla can result in Wallenberg syndrome, which is characterized by vertigo/nystagmus, ipsilateral cerebellar signs (eg, ataxia, dysmetria), loss of pain/temperature sensation in the ipsilateral face and contralateral body, bulbar weakness (eg, dysphagia), and ipsilateral Horner syndrome (miosis, ptosis, anhidrosis).

**Educational objective:**
Ischemic injury to the bilateral ventral pons can lead to locked-in syndrome, a condition in which patients are unable to move or speak (due to interruption of the corticospinal and corticobulbar tracts) but retain



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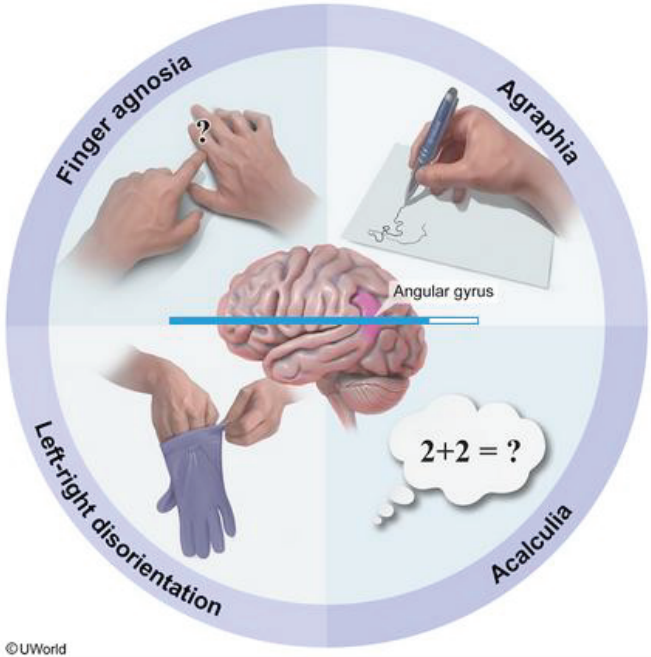
Gerstmann syndrome

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are unable to move or speak (due to interruption of the corticospinal and corticobulbar tracts) but retain



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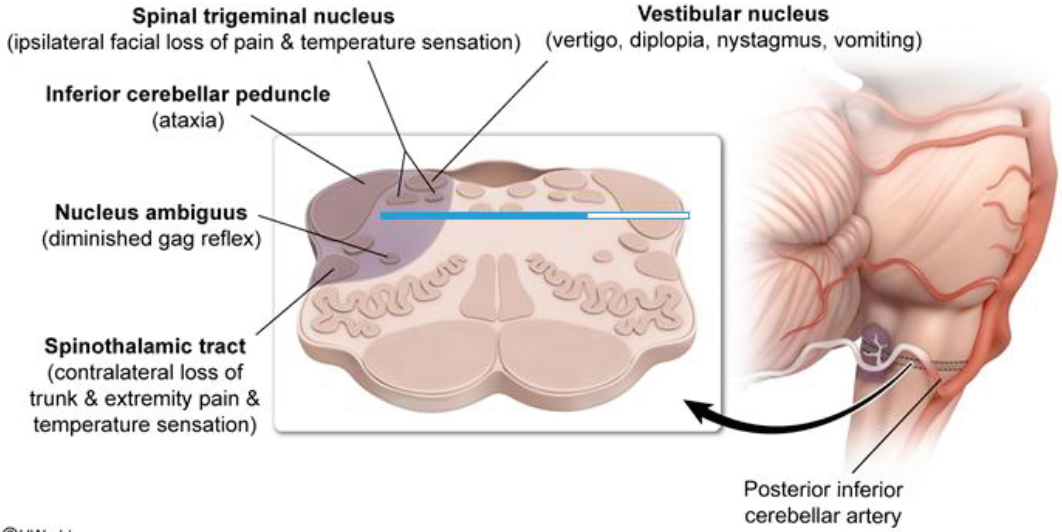
## Lateral medullary (Wallenberg) syndrome

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are unable to move or speak (due to interruption of the corticospinal and corticobulbar tracts) but retain



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disorientation.

**(Choice B)** Damage to the cingulate gyrus can result in significant behavioral symptoms (eg, abulia).

**(Choice E)** Damage to the medial medulla can result in contralateral hemiparesis (due to damage of the lateral corticospinal tract), contralateral hemisensory loss (dorsal column/medial lemniscal pathway), and ipsilateral tongue paralysis (hypoglossal nucleus).

**(Choice F)** Damage to the lateral medulla can result in Wallenberg syndrome, which is characterized by vertigo/nystagmus, ipsilateral cerebellar signs (eg, ataxia, dysmetria), loss of pain/temperature sensation in the ipsilateral face and contralateral body, bulbar weakness (eg, dysphagia), and ipsilateral Horner syndrome (miosis, ptosis, anhidrosis).

**Educational objective:**
Ischemic injury to the bilateral ventral pons can lead to locked-in syndrome, a condition in which patients are unable to move or speak (due to interruption of the corticospinal and corticobulbar tracts) but retain consciousness, sensation, eye opening, and vertical eye movements.

| Anatomy | Nervous System | Ischemic stroke |
|---|---|---|
| Subject | System | Topic |



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A 4-year-old Caucasian boy is evaluated for difficulty walking. Past medical history includes frequent respiratory infections. Cultured cells from this patient demonstrate a high rate of radiation-induced genetic mutation. This patient is most likely to experience which of the following?

A. Neurofibrillary tangles in neocortex
B. Cerebellar atrophy
C. Loss of neurons in the substantia nigra
D. Atrophy of caudate nucleus
E. Posterior column degeneration
F. Presence of Lewy bodies

Submit



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A 4-year-old Caucasian boy is evaluated for difficulty walking. Past medical history includes frequent respiratory infections. Cultured cells from this patient demonstrate a high rate of radiation-induced genetic mutation. This patient is most likely to experience which of the following?

A. Neurofibrillary tangles in neocortex (5%)
B. Cerebellar atrophy (56%)
C. ~~Loss of neurons in the substantia nigra~~ (3%)
D. ~~Atrophy of caudate nucleus~~ (6%)
E. Posterior column degeneration (24%)
F. ~~Presence of Lewy bodies~~ (4%)

Incorrect
Correct answer
B

56%
Answered correctly

01 min, 09 secs
Time Spent

01/30/2021
Last Updated



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Ataxia-telangiectasia is an autosomal recessive disorder. Cerebellar atrophy leads to the **ataxia** that occurs in the first years of life. (**Oculocutaneous telangiectasia** is another manifestation, but is usually delayed. Telangiectasias are abnormal dilatations of capillary vessels.) Patients with ataxia-telangiectasia also have severe immunodeficiency with **repeated sinopulmonary infections**. The risk of **cancer** in these patients is increased significantly because of inefficient DNA repair.

DNA damage and repair is an ongoing process. A lot of naturally-occurring agents cause DNA damage: sunlight, UV light, ionizing radiation (gamma and X-ray), and free oxygen radicals are produced during the cell cycle. Some chemicals (hydrocarbons in cigarette smoke, aflatoxins produced by moldy peanuts) are also harmful to DNA. DNA repair occurs continuously by means of direct reversal of damage, base and nucleotide excision repair, and mismatch repair.

A number of inherited disorders are caused by deficient DNA-repair enzymes:

1. Ataxia-telangiectasia is characterized by DNA hypersensitivity to ionizing radiation.
2. In xeroderma pigmentosum, DNA is hypersensitive to UV radiation, causing premature skin aging and increased risk of skin cancer (malignant melanoma and squamous cell carcinoma).
3. Fanconi anemia is caused by hypersensitivity of DNA to cross-linking agents.


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2. In xeroderma pigmentosum, DNA is hypersensitive to UV radiation, causing premature skin aging and increased risk of skin cancer (malignant melanoma and squamous cell carcinoma).
3. Fanconi anemia is caused by hypersensitivity of DNA to cross-linking agents.
4. Bloom syndrome is characterized by generalized chromosomal instability. Increased susceptibility to neoplasms is present.
5. Hereditary nonpolyposis colorectal cancer (HNPCC) occurs due to a defect in DNA mismatch-repair enzymes. It leads to increased susceptibility to colon cancer.

**(Choice A)** Neurofibrillary tangles in the neocortex are seen in Alzheimer disease.

**(Choice C)** Loss of neurons in the substantia nigra is characteristic of Parkinson disease.

**(Choice D)** Atrophy of caudate nucleus is seen in Huntington disease.

**(Choice E)** Posterior column involvement is seen with both vitamin B 12 deficiency and syphilis.

**(Choice F)** The presence of Lewy bodies is characteristic of Parkinsonism.

**Educational Objective:**
Ataxia-telangiectasia is an autosomal-recessive disorder resulting from a defect in DNA-repair genes. The DNA of these patients is hypersensitive to ionizing radiation. Manifestations include cerebellar ataxia, oculocutaneous telangiectasias, repeated sinopulmonary infections, and an increased incidence of


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5. Hereditary nonpolyposis colorectal cancer (HNPCC) occurs due to a defect in DNA mismatch-repair enzymes. It leads to increased susceptibility to colon cancer.

**(Choice A)** Neurofibrillary tangles in the neocortex are seen in Alzheimer disease.

**(Choice C)** Loss of neurons in the substantia nigra is characteristic of Parkinson disease.

**(Choice D)** Atrophy of caudate nucleus is seen in Huntington disease.

**(Choice E)** Posterior column involvement is seen with both vitamin B 12 deficiency and syphilis.

**(Choice F)** The presence of Lewy bodies is characteristic of Parkinsonism.

**Educational Objective:**
Ataxia-telangiectasia is an autosomal-recessive disorder resulting from a defect in DNA-repair genes. The DNA of these patients is hypersensitive to ionizing radiation. Manifestations include cerebellar ataxia, oculocutaneous telangiectasias, repeated sinopulmonary infections, and an increased incidence of malignancy.

| Pathology | Nervous System | Ataxia telangiectasia |
|---|---|---|
| Subject | System | Topic |


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A 72-year-old woman is brought to the office due to forgetfulness. Her family has noticed that the patient quickly forgets conversations and misplaces household items. The symptoms have progressively worsened over the past 2-3 years. A month ago, the patient became lost while driving in the neighborhood where she has lived most of her adult life. She has no significant medical history, and her only medication is a daily multivitamin. The patient does not use tobacco, alcohol, or illicit drugs and lives with her son and his wife. Vital signs are within normal limits. On physical examination, the patient has a short-term memory deficit with no other significant neurologic findings. After discussion, an oral cholinesterase inhibitor is prescribed. Which of the following is the most likely effect of the drug prescribed for this patient?

A. Delayed disease progression due to a neuroprotective effect
B. Improved cognitive function with no change in disease course
C. Neuroprotection with no effect on cognitive performance
D. Reversal of cognitive decline due to increased neuroplasticity
E. Symptomatic improvement only through the placebo effect


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quickly forgets conversations and misplaces household items. The symptoms have progressively worsened over the past 2-3 years. A month ago, the patient became lost while driving in the neighborhood where she has lived most of her adult life. She has no significant medical history, and her only medication is a daily multivitamin. The patient does not use tobacco, alcohol, or illicit drugs and lives with her son and his wife. Vital signs are within normal limits. On physical examination, the patient has a short-term memory deficit with no other significant neurologic findings. After discussion, an oral cholinesterase inhibitor is prescribed. Which of the following is the most likely effect of the drug prescribed for this patient?

A. ~~Delayed disease progression due to a neuroprotective effect~~ (27%)

✓ B. Improved cognitive function with no change in disease course (67%)

C. ~~Neuroprotection with no effect on cognitive performance~~ (3%)

D. Reversal of cognitive decline due to increased neuroplasticity (0%)

E. ~~Symptomatic improvement only through the placebo effect~~ (0%)

Correct

67%

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| Alzheimer disease | |
|---|---|
| **Pathogenesis** | • β-amyloid ↔ neuronal stress → excitotoxicity (glutamatergic NMDA overactivity) → neuronal degeneration → diffuse cortical atrophy<br>• Loss of cholinergic neurons → impaired memory & cognition |
| **Clinical features** | • Most common dementia; age >65 years<br>• Deficits affecting multiple cortical domains<br>◦ Memory (especially for recent events)<br>◦ Executive function (eg, planning)<br>◦ Visuospatial (eg, getting lost)<br>◦ Language (eg, poverty of speech)<br>◦ Motor (eg, gait apraxia leading to falls) |
| **Symptomatic management** | • NMDA receptor antagonist (memantine)<br>• Cholinesterase inhibitors (eg, donepezil, galantamine) |

This elderly patient with an insidious onset of increasing forgetfulness, visuospatial deficits (eg, misplacing objects), and executive dysfunction (eg, getting lost in familiar surroundings), coupled with a normal


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| | |
|---|---|
| Management | • Cholinesterase inhibitors (eg, donepezil, galantamine) |

This elderly patient with an insidious onset of increasing forgetfulness, visuospatial deficits (eg, misplacing objects), and executive dysfunction (eg, getting lost in familiar surroundings), coupled with a normal neurologic examination, most likely has **Alzheimer disease** (AD).

**Degeneration of cholinergic neurons**, resulting in reduced acetylcholine synthesis in the basal forebrain, contributes to the memory loss and executive dysfunction that characterizes AD. **Cholinesterase inhibitors** (eg, donepezil, rivastigmine, galantamine) block acetylcholinesterase in the synaptic cleft to compensate for the loss of cholinergic transmission.

Although cholinesterase inhibitors provide modest **symptomatic improvement**, they do not enhance neuron survival. Therefore, they are **not** considered **neuroprotective** and do not impact the overall trajectory of AD. In contrast, NMDA receptor antagonists (eg, memantine) inhibit glutamate NMDA signaling to prevent excitotoxicity (calcium overload) and subsequent neuronal apoptosis; these agents likely serve a neuroprotective role that may slow disease progression **(Choice A)**.

**(Choice C)** Antioxidants (eg, vitamin E) may delay progression of AD through a neuroprotective effect but do not seem to improve cognition.

**(Choice D)** Neuroplasticity, the ability of neurons to reorganize or restructure, is most notably prominent in


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likely serve a neuroprotective role that may slow disease progression **(Choice A)**.

**(Choice C)** Antioxidants (eg, vitamin E) may delay progression of AD through a neuroprotective effect but do not seem to improve cognition.

**(Choice D)** Neuroplasticity, the ability of neurons to reorganize or restructure, is most notably prominent in childhood. Reduced neuroplasticity has been implicated in multiple neuropsychiatric conditions (eg, psychosis). However, currently available medications for AD cannot enhance neuroplasticity.

**(Choice E)** Cholinesterase inhibitors have demonstrated greater improvement in cognition and daily functioning compared to placebo.

**Educational objective:**
Cholinesterase inhibitors (eg, donepezil, galantamine) may provide modest symptomatic improvement of cognitive symptoms and temporarily improve functioning in patients with Alzheimer disease. However, these medications do not alter the inevitable disease progression.

**References**

- Current understanding of Alzheimer's disease diagnosis and treatment.


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A 34-year-old woman comes to the office due to a 2-day history of reduced sensation in her legs. Lately, the patient has also had significant fatigue, especially with exercise. Six months ago, she had an episode of visual blurring that resolved spontaneously after a few days. Medical history is significant for psoriasis, for which she uses a topical glucocorticoid ointment. The patient does not use tobacco or illicit drugs. Vital signs are normal. Examination indicates decreased pain and light touch perception in both legs below the level of the umbilicus. Mild bilateral spasticity is noted. Which of the following pathologic brain lesions is most specific for this patient's disease process?

A. Microglial nodules
B. Neuritic plaques and neurofibrillary tangles
C. Perivenular inflammatory cells
D. Spongiform changes
E. Viral inclusions

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A 34-year-old woman comes to the office due to a 2-day history of reduced sensation in her legs. Lately, the patient has also had significant fatigue, especially with exercise. Six months ago, she had an episode of visual blurring that resolved spontaneously after a few days. Medical history is significant for psoriasis, for which she uses a topical glucocorticoid ointment. The patient does not use tobacco or illicit drugs. Vital signs are normal. Examination indicates decreased pain and light touch perception in both legs below the level of the umbilicus. Mild bilateral spasticity is noted. Which of the following pathologic brain lesions is most specific for this patient's disease process?

- A. Microglial nodules (26%)
- B. Neuritic plaques and neurofibrillary tangles (3%)
- C. Perivenular inflammatory cells (59%)
- D. Spongiform changes (3%)
- E. Viral inclusions (5%)

Incorrect



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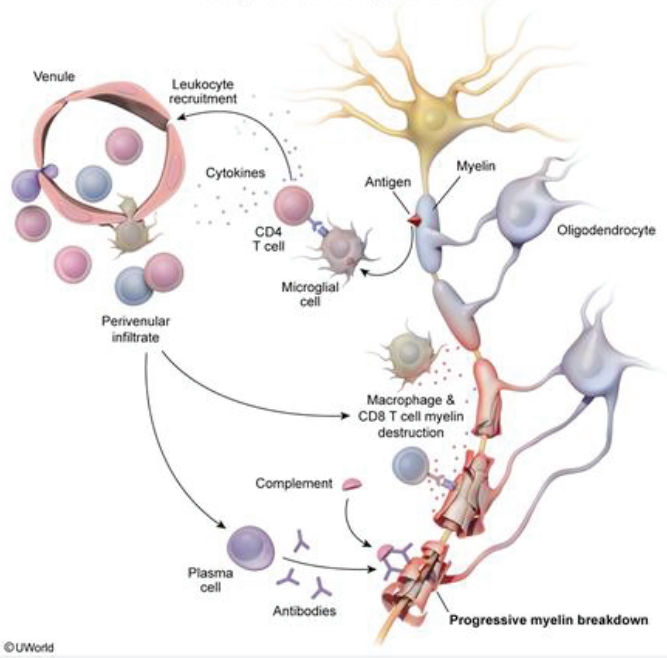
Pathogenesis of multiple sclerosis

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Reduced sensation and spasticity in the lower extremities suggest a lesion in the spinal cord. This, in conjunction with this patient's prior episode of blurred vision and her severe fatigue with exercise (Uhthoff's phenomenon), makes **multiple sclerosis** (MS) a likely diagnosis. MS is an immune-mediated disorder of the central nervous system (CNS), characterized by focal lesions of demyelination. Patients have various neurologic deficits that wax and wane (symptoms are disseminated across time and space).

Histologically, active MS plaques are characterized by **perivenular inflammatory infiltrates** made up primarily of autoreactive T lymphocytes and macrophages directed against myelin components. Extensive inflammation damages the blood-brain barrier, increasing inflammatory cell recruitment into the CNS (with the vessel wall remaining intact, unlike in CNS vasculitis). Infiltrating **macrophages containing myelin debris** are seen throughout the lesion, and recruitment of B lymphocytes to the perivascular spaces leads to the formation of myelin-specific antibodies. **Patchy demyelination** occurs, and while axons are typically spared, significant or prolonged disease may result in neuron death. Residual chronic findings include hypertrophy and hyperplasia of astrocytes (glial scarring).

**(Choice A)** Microglial nodules are nonspecific findings that can be seen in patients with MS, as well as in those with HIV encephalopathy and other viral infections. They are thought to be reactive lesions that



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**(Choice A)** Microglial nodules are nonspecific findings that can be seen in patients with MS, as well as in those with HIV encephalopathy and other viral infections. They are thought to be reactive lesions that occur in the setting of inflammation, rather than a specific pathologic finding.

**(Choice B)** Neuritic plaques and neurofibrillary tangles (tau protein) are characteristic findings in Alzheimer disease, which presents with memory impairment, not focal neurologic deficits, and is rare in young patients.

**(Choice D)** Spongiform encephalopathy is seen in prion diseases (eg, bovine spongiform encephalopathy, Creutzfeldt-Jakob disease). Patients present with rapid-onset dementia, myoclonus, and ataxia. Episodic or waxing and waning symptoms are more consistent with MS.

**(Choice E)** Negri bodies are viral inclusions in the cytoplasm of nerve cells in patients with rabies. Rabies occurs after a bite from an infected animal and presents with tingling or irritation at the inoculation site followed by hydrophobia, delirium, coma, and death. This disease is typically fatal within days of symptom presentation and would not be expected to cause focal abnormalities over a period of months.

**Educational objective:**
Multiple sclerosis is an immune-mediated disorder of the central nervous system characterized by focal


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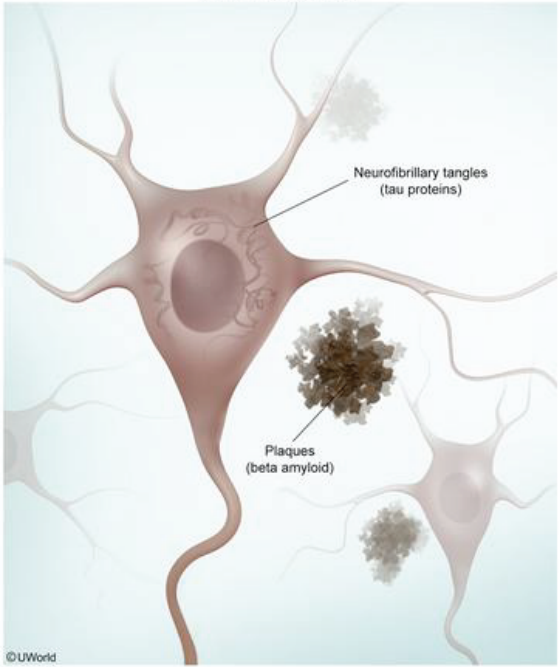
Alzheimer disease

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young patients.

**(Choice D)** Spongiform encephalopathy is seen in prion diseases (eg, bovine spongiform encephalopathy, Creutzfeldt-Jakob disease). Patients present with rapid-onset dementia, myoclonus, and ataxia. Episodic or waxing and waning symptoms are more consistent with MS.

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**Educational objective:**
Multiple sclerosis is an immune-mediated disorder of the central nervous system characterized by focal demyelination (plaques). Histologically, plaques contain foci of perivenular inflammatory infiltrates made up primarily of autoreactive T lymphocytes and macrophages. Patchy demyelination occurs followed by astrocyte hyperplasia (glial scarring).

| Pathology | Nervous System | Multiple sclerosis |
|---|---|---|
| Subject | System | Topic |

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A 72-year-old man comes to the office due to poor sleep. He is concerned that he is sleeping less since he retired a year ago. He says, "I used to sleep a solid 8 hours, but now I wake up several times a night. And I'm up for the day between 5:00 and 6:00 AM, which is a full hour before I want to get up. I'm probably only getting about 6 or 7 hours of sleep total." The patient typically falls asleep while watching television at 10:00 PM. He sometimes awakens to use the bathroom in the middle of the night but typically falls back asleep within 15 minutes. The patient likes to do crosswords and play golf in the mornings but occasionally takes 30-minute naps in the afternoon. The patient's wife says that he snores softly, but she has not witnessed any breathing pauses. Medical problems include hypertension and a history of depression. The patient does not use alcohol or illicit drugs. Which of the following is the most likely cause of this patient's symptoms?

A. Adjustment disorder
B. Age-related sleep changes
C. Insomnia disorder
D. Major depressive disorder
E. Obstructive sleep apnea



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getting about 6 or 7 hours of sleep total. The patient typically falls asleep while watching television at 10:00 PM. He sometimes awakens to use the bathroom in the middle of the night but typically falls back asleep within 15 minutes. The patient likes to do crosswords and play golf in the mornings but occasionally takes 30-minute naps in the afternoon. The patient's wife says that he snores softly, but she has not witnessed any breathing pauses. Medical problems include hypertension and a history of depression. The patient does not use alcohol or illicit drugs. Which of the following is the most likely cause of this patient's symptoms?

- A. Adjustment disorder
- B. Age-related sleep changes
- C. Insomnia disorder
- D. Major depressive disorder
- E. Obstructive sleep apnea
- F. REM sleep behavior disorder

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getting about 6 or 7 hours of sleep total. The patient typically falls asleep while watching television at 10:00 PM. He sometimes awakens to use the bathroom in the middle of the night but typically falls back asleep within 15 minutes. The patient likes to do crosswords and play golf in the mornings but occasionally takes 30-minute naps in the afternoon. The patient's wife says that he snores softly, but she has not witnessed any breathing pauses. Medical problems include hypertension and a history of depression. The patient does not use alcohol or illicit drugs. Which of the following is the most likely cause of this patient's symptoms?

- A. Adjustment disorder (3%)
- ✓ B. Age-related sleep changes (90%)
- C. Insomnia disorder (1%)
- D. Major depressive disorder (1%)
- E. Obstructive sleep apnea (1%)
- F. REM sleep behavior disorder (2%)


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This patient's sleep changes are consistent with **normal aging**. Age-related changes in sleep architecture include **decreased total sleep time** and slow-wave sleep with increased nighttime sleep latency. As a result of these changes, elderly patients may experience more **fragmented sleep** with nocturnal awakenings and an **earlier wake-up time** when compared to their previous sleep pattern. All these changes can in turn lead to subjective reports of insomnia and intentional and unintentional **daytime napping**.

This patient functions well during the daytime and does not exhibit any other symptoms that would be concerning for a sleep disorder (eg, sleep apnea). He should be reassured that these changes are normal.

(**Choice A**) Adjustment disorder should be considered in a patient who develops mood symptoms within 3 months of a stressor. If mood symptoms persist for >6 months after the stressor, then adjustment disorder cannot be diagnosed. This patient does not have any mood symptoms, and his retirement was >6 months ago.

**(Choice C)** Insomnia disorder involves persistent difficulties initiating or maintaining sleep, resulting in clinically significant distress or impairment. It would not be diagnosed in a patient with normal age-related sleep changes.


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**(Choice C)** Insomnia disorder involves persistent difficulties initiating or maintaining sleep, resulting in clinically significant distress or impairment. It would not be diagnosed in a patient with normal age-related sleep changes.

**(Choice D)** Although sleep changes are frequent in major depressive disorder, this patient lacks other key depressive symptoms necessary to meet criteria for it (eg, sadness, decreased interest, anhedonia, decreased appetite, suicidality).

**(Choice E)** Sleep apnea is associated with hypertension and fragmented sleep. However, this patient has no history of witnessed apneas and his sleep changes are classic for normal aging.

**(Choice F)** REM sleep behavior disorder is a parasomnia characterized by dream-enactment behaviors that occur due to loss of normal REM sleep atonia.

**Educational objective:**
Age-related sleep changes may be reported as insomnia and must be differentiated from primary sleep disorders and other disorders. Normal changes include decreased total sleep time, increased nighttime awakenings, sleepiness earlier in the evening with earlier morning awakening, and increased daytime napping.

**References**



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**(Choice C)** Insomn
clinically significant
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decreased appetite

**(Choice E)** Sleep
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**(Choice F)** REM s
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**Educational objec**
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**References**

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| Major depressive disorder | |
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| **Diagnosis** | • ≥5 of the following symptoms lasting ≥2 weeks (at least 1 symptom must be either depressed mood or loss of interest/pleasure):<br>◦ Depressed mood<br>◦ Loss of interest or pleasure<br>◦ Change in appetite or weight<br>◦ Insomnia or hypersomnia<br>◦ Psychomotor retardation or agitation<br>◦ Low energy<br>◦ Poor concentration or indecisiveness<br>◦ Thoughts of worthlessness or inappropriate guilt<br>◦ Recurrent thoughts of death or suicide<br>• No history of mania or hypomania<br>• Not due to substances or another medical condition |
| **Treatment** | • Psychotherapy<br>• Antidepressant medication |

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A 65-year-old man is found dead at his home due to a suspected suicide. The family reports that the patient has been having difficulty swallowing, dyspnea on exertion, and arm and leg weakness for the past several months and had undergone a medical workup. They suspect the physician may have given bad news and the patient ended his life so he would not have to live with the diagnosed condition. External examination shows atrophy of the muscles of the right lower and left upper extremities. Autopsy would most likely reveal which of the following additional findings?

A. Degeneration of dorsal spinal roots
B. Diaphragmatic atrophy
C. Diffuse brain atrophy
D. Inflammatory infiltrates in skeletal muscles
E. Plaques and gliosis in periventricular white matter

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A 65-year-old man is found dead at his home due to a suspected suicide. The family reports that the patient has been having difficulty swallowing, dyspnea on exertion, and arm and leg weakness for the past several months and had undergone a medical workup. They suspect the physician may have given bad news and the patient ended his life so he would not have to live with the diagnosed condition. External examination shows atrophy of the muscles of the right lower and left upper extremities. Autopsy would most likely reveal which of the following additional findings?

A. ~~Degeneration of dorsal spinal roots~~ (17%)

✓ B. ~~Diaphragmatic atrophy~~ (49%)

C. ~~Diffuse brain atrophy~~ (6%)

D. ~~Inflammatory infiltrates in skeletal muscles~~ (6%)

✗ E. Plaques and gliosis in periventricular white matter (20%)

Incorrect
Correct answer
B

49%
Answered correctly

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11/06/2020
Last Updated



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| Amyotrophic lateral sclerosis | |
|---|---|
| **Criteria** | **Description** |
| **Macroscopic** | • Thin anterior roots<br>• Mild atrophy of the precentral gyrus (primary motor cortex) |
| **Microscopic** | • Loss of neurons in the anterior horn (LMN lesion)<br>• Degeneration & atrophy of the lateral corticospinal tracts (UMN lesion)<br>• Loss of neurons in the motor nuclei of CNs V, IX, X & XII<br>• Muscle: denervation atrophy (small, angular fibers) |
| **Clinical** | • LMN symptoms: muscle atrophy & fasciculation<br>• UMN symptoms: spasticity, hyperreflexia & |


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| **Clinical** | • LMN symptoms: muscle atrophy & fasciculation<br>• UMN symptoms: spasticity, hyperreflexia & pathologic reflexes |
| **Genetic** | • Mutation of copper-zinc superoxide dismutase (SOD1) gene may be implicated |
| **Treatment** | • Riluzole (mechanism of action: decreased glutamate release) |

**LMN** = lower motor neuron; **UMN** = upper motor neuron.

This patient with a history of bulbar symptoms (eg, difficulty swallowing) and limb weakness has postmortem evidence of asymmetric muscular atrophy. This presentation is concerning for **amyotrophic lateral sclerosis** (ALS), a progressive, fatal neurodegenerative disease of both upper motor neurons (UMNs) and lower motor neurons (LMNs).

ALS has the highest incidence in patients age 60-75. The most common initial presentation includes **asymmetric weakness** of the extremities; bulbar symptoms are also common and can include dysphagia and dysarthria. Because any upper or lower motor neuron can be affected, the initial presentation may


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and dysarthria. Because any upper or lower motor neuron can be affected, the initial presentation may vary widely. UMN degeneration leads to spasticity and hyperreflexia; **LMN degeneration** leads to denervation **atrophy of skeletal muscles**.

The most concerning site of LMN degeneration involves the **diaphragm** because it results in **dyspnea**, as reported by this patient, and eventual **respiratory failure**. Diaphragmatic function can be monitored with imaging studies (eg, ultrasound) and via testing of respiratory muscle strength (eg, sniff tests); postmortem studies typically demonstrate striking **diaphragmatic atrophy**.

**(Choice A)** Degeneration of dorsal spinal roots would lead to sensory dysfunction, not motor dysfunction, as seen in this patient. Sensory dysfunction is not a classic feature of ALS.

**(Choice C)** Because ALS results primarily in neurodegeneration of motor neurons, atrophy is seen predominately in the motor cortex rather than diffusely throughout the brain.

**(Choice D)** Inflammatory infiltrates in skeletal muscles are seen in inflammatory myopathies, including dermatomyositis and polymyositis. Long-standing disease can lead to muscle atrophy; however, ALS causes muscle atrophy due to denervation rather than inflammation.

**(Choice E)** Plaques and gliosis in periventricular white matter are characteristic pathologic findings of multiple sclerosis. These inflammatory demyelinating lesions occur in the CNS; therefore, weakness is


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predominately in the motor cortex rather than diffusely throughout the brain.

**(Choice D)** Inflammatory infiltrates in skeletal muscles are seen in inflammatory myopathies, including dermatomyositis and polymyositis. Long-standing disease can lead to muscle atrophy; however, ALS causes muscle atrophy due to denervation rather than inflammation.

**(Choice E)** Plaques and gliosis in periventricular white matter are characteristic pathologic findings of multiple sclerosis. These inflammatory demyelinating lesions occur in the CNS; therefore, weakness is often associated with spasticity (UMN sign) rather than atrophy (LMN sign). In addition, it typically occurs in younger women (age <55).

**Educational objective:**
Amyotrophic lateral sclerosis causes degeneration of both upper and lower motor neurons and can result in bulbar and skeletal muscle weakness. Denervation atrophy can affect the diaphragm and contribute to respiratory failure.

| Pathology | Nervous System | Amyotrophic lateral sclerosis |
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A 59-year-old man comes to the office due to diplopia and a drooping right eyelid. His symptoms began a day earlier and have since worsened. Physical examination shows a dilated right pupil that is nonreactive to both light and accommodation. There is vertical and horizontal diplopia. When the patient is asked to stare straight ahead, the right eye is directed inferiorly and laterally with respect to the left eye. MRI of the brain reveals an aneurysm involving the right posterior communicating artery. Which of the following muscles is most likely to remain functionally intact in this patient?

A. Inferior oblique
B. Inferior rectus
C. Lateral rectus
D. Levator palpebrae
E. Medial rectus
F. Superior rectus

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A 59-year-old man comes to the office due to diplopia and a drooping right eyelid. His symptoms began a day earlier and have since worsened. Physical examination shows a dilated right pupil that is nonreactive to both light and accommodation. There is vertical and horizontal diplopia. When the patient is asked to stare straight ahead, the right eye is directed inferiorly and laterally with respect to the left eye. MRI of the brain reveals an aneurysm involving the right posterior communicating artery. Which of the following muscles is most likely to remain functionally intact in this patient?

- A. Inferior oblique (5%)
- B. Inferior rectus (1%)
- ✓ C. Lateral rectus (86%)
- D. Levator palpebrae (2%)
- E. Medial rectus (1%)
- F. Superior rectus (2%)


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| Nerve | Eye muscle(s) innervated | Oculomotor functions | Lesion findings |
|---|---|---|---|
| **Oculomotor (CN III)** | • Superior rectus<br>• Medial rectus<br>• Inferior rectus<br>• Inferior oblique<br>• Levator palpebrae superioris | • Adduction<br>• Depression<br>• Elevation<br>• External rotation | • Eye deviated downward & laterally<br>• Diagonal diplopia<br>• Dilation of pupil & loss of accommodation<br>• Ptosis |
| **Trochlear (CN IV)** | • Superior oblique | • Abduction<br>• Internal rotation<br>• Depression while adducted | • Eye deviated upward<br>• Vertical & torsional diplopia |
| **Abducens (CN VI)** | • Lateral rectus | • Abduction | • Eye deviated medially<br>• Horizontal diplopia |


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This patient has a right **oculomotor nerve (CN III) palsy** secondary to a compressive aneurysm. Lesions involving CN III cause ptosis (drooping of the upper eyelid) and impair adduction, depression, and elevation of the eye. As a result, diagonal (eg, horizontal and vertical) diplopia is frequently present. The eye rests in a **"down and out" position** due to the unopposed action of the **superior oblique** (CN IV) and **lateral rectus** (CN VI) muscles. Pupillary constriction and accommodation can also be affected as CN III carries parasympathetic fibers to the ciliary muscle and the iris sphincter.

CN III palsy can be due to a variety of causes, including intracranial tumors or aneurysms, nerve ischemia, and head trauma. Aneurysms causing CN III palsy most often involve the **posterior communicating artery**. When due to an aneurysm, symptoms that develop acutely are especially worrisome as they suggest active aneurysmal dilation and possible impending rupture.

**(Choices A, B, D, E, and F)** All of these muscles are innervated by CN III, so their function will be impaired in this patient.

**Educational objective:**
Lesions involving the oculomotor nerve (CN III) cause ptosis, a downward and laterally deviated eye, impaired pupillary constriction and accommodation, and diagonal diplopia. The most dreaded cause of CN III palsy is an enlarging intracranial aneurysm.



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in a **"down and out" position** due to the unopposed action of the **superior oblique** (CN IV) and **lateral rectus** (CN VI) muscles. Pupillary constriction and accommodation can also be affected as CN III carries parasympathetic fibers to the ciliary muscle and the iris sphincter.

CN III palsy can be due to a variety of causes, including intracranial tumors or aneurysms, nerve ischemia, and head trauma. Aneurysms causing CN III palsy most often involve the **posterior communicating artery**. When due to an aneurysm, symptoms that develop acutely are especially worrisome as they suggest active aneurysmal dilation and possible impending rupture.

**(Choices A, B, D, E, and F)** All of these muscles are innervated by CN III, so their function will be impaired in this patient.

**Educational objective:**
Lesions involving the oculomotor nerve (CN III) cause ptosis, a downward and laterally deviated eye, impaired pupillary constriction and accommodation, and diagonal diplopia. The most dreaded cause of CN III palsy is an enlarging intracranial aneurysm.

| Anatomy | Nervous System | Cranial nerve palsy |
|---|---|---|
| Subject | System | Topic |

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A 28-year-old man is undergoing a laparoscopic appendectomy for acute appendicitis. Shortly after induction of anesthesia, the surgeon reports difficulty maintaining abdominal insufflation due to severe muscle rigidity. Pulse is 130/min and the ECG tracing shows sinus tachycardia. Physical examination reveals diffuse muscle stiffness. Inhibition of which of the following is most likely to improve this patient's condition?

A. Acetylcholine degradation in cholinergic synapses
B. Alpha-receptor–mediated sympathetic activity
C. GABA-mediated neuron hyperpolarization
D. Ligand-receptor interaction in cholinergic synapses
E. Sarcoplasmic calcium release in skeletal muscles

Submit


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A 28-year-old man is undergoing a laparoscopic appendectomy for acute appendicitis. Shortly after induction of anesthesia, the surgeon reports difficulty maintaining abdominal insufflation due to severe muscle rigidity. Pulse is 130/min and the ECG tracing shows sinus tachycardia. Physical examination reveals diffuse muscle stiffness. Inhibition of which of the following is most likely to improve this patient's condition?

A. Acetylcholine degradation in cholinergic synapses (10%)
B. Alpha-receptor–mediated sympathetic activity (1%)
C. GABA-mediated neuron hyperpolarization (3%)
D. Ligand-receptor interaction in cholinergic synapses (10%)
✓ E. Sarcoplasmic calcium release in skeletal muscles (73%)

Correct

73%
Answered correctly

02 mins, 30 secs
Time Spent

09/29/2020
Last Updated



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| Malignant hyperthermia | |
|---|---|
| **Pathophysiology** | • Genetic mutation of ryanodine receptors<br>• Triggered by inhalational anesthetics & succinylcholine<br>• Unregulated sarcoplasmic calcium release → sustained muscle contraction |
| **Clinical manifestations** | • Masseter muscle spasm<br>• Widespread muscle contraction (rigidity)<br>• Hypercarbia<br>• Rhabdomyolysis → hyperkalemia & acute renal failure<br>• Hyperthermia (late manifestation) |
| **Treatment** | • Immediate cessation of causative anesthetic<br>• Dantrolene |

During laparoscopic procedures, small incisions are created to insert instruments into the abdominal cavity. Gas is insufflated to allow better visualization and easier access to organs while operating. Difficulty


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During laparoscopic procedures, small incisions are created to insert instruments into the abdominal cavity. Gas is insufflated to allow better visualization and easier access to organs while operating. Difficulty maintaining abdominal insufflation due to muscle contraction is often caused by insufficient doses of paralytic agents. However, if the patient has been appropriately medicated, sustained muscle contraction, especially when widespread, may be due to **malignant hyperthermia** (MH).

MH is often due to abnormal ryanodine receptors (*RYR1*) in the skeletal muscle. On exposure to certain anesthetic agents (typically succinylcholine and inhalational gases), these abnormal receptors allow the unregulated passage of calcium from the sarcoplasmic reticulum into the intracellular space. As a result of excessive calcium accumulation, patients develop sudden-onset, **widespread muscle rigidity**. Sustained muscle contraction **produces excessive $CO_2$**, leading to hypercarbia and acidosis; depletes cellular oxygen, leading to lactic acid production; and causes **muscle breakdown**, leading to rhabdomyolysis. **Hyperthermia** is often a later clinical sign that develops as the increased cellular metabolism overwhelms the body's ability to dissipate heat.

Many pharmacologic muscle relaxants work upstream from the pathologic process of excessive calcium release and are therefore ineffective during an acute MH crisis. **Dantrolene** is used to treat MH because it directly **inhibits intracellular calcium release** from the abnormal ryanodine receptor (*RYR1*).


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directly **inhibits intracellular calcium release** from the abnormal ryanodine receptor (*RYR1*).

**(Choice A)** Neostigmine is an acetylcholinesterase inhibitor that prevents the degradation of acetylcholine in the neuromuscular junction. Therefore, it could increase, rather than decrease, the strength of muscle contractions.

**(Choice B)** Alpha-adrenergic antagonists (eg, phentolamine, phenoxybenzamine) inhibit alpha-receptor–mediated sympathetic activity. They are used primarily to lower blood pressure by decreasing vascular tone; they have minimal effect on skeletal muscle.

**(Choices C and D)** Baclofen is a GABA-B agonist that increases neuron hyperpolarization in the CNS to relax muscles. Nondepolarizing neuromuscular blocking agents (eg, rocuronium) are nicotinic receptor antagonists that inhibit the action of acetylcholine at the motor endplate. Both agents work upstream from intracellular calcium release and therefore have minimal impact on muscle contraction during an MH crisis.

**Educational objective:**
Malignant hyperthermia presents with widespread muscle rigidity after administration of inhalation anesthetics and/or succinylcholine to genetically susceptible individuals. It is treated with dantrolene, which blocks ryanodine receptors to prevent the release of calcium from the sarcoplasmic reticulum into the cytoplasm of skeletal muscle fibers.


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A newly developed inhaled anesthetic has an improved safety profile compared to traditional fluorinated anesthetics. Preliminary pharmacodynamic properties of the agent are determined through a series of experiments on human volunteers. The tests show that the agent demonstrates relatively high potency. Which of the following parameters best correlates with the potency of an inhaled anesthetic?

A. Arteriovenous concentration gradient
B. Blood/gas partition coefficient
C. Hepatic metabolism rate
D. Minimal alveolar concentration
E. Steepness of arterial tension curve

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A newly developed inhaled anesthetic has an improved safety profile compared to traditional fluorinated anesthetics. Preliminary pharmacodynamic properties of the agent are determined through a series of experiments on human volunteers. The tests show that the agent demonstrates relatively high potency. Which of the following parameters best correlates with the potency of an inhaled anesthetic?

A. Arteriovenous concentration gradient (5%)
B. ~~Blood/gas partition coefficient~~ (22%)
C. ~~Hepatic metabolism rate~~ (1%)
D. Minimal alveolar concentration (68%)
E. ~~Steepness of arterial tension curve~~ (1%)

Correct

68%
Answered correctly

02 mins, 06 secs
Time Spent

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Explanation



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The potency of an inhaled anesthetic is determined by the minimum concentration in the brain necessary to achieve an adequate level of anesthesia. When an inhaled anesthetic is administered at a constant rate over a prolonged period of time, its partial pressure in the brain equals its partial pressure in the other compartments (inhaled air, lungs, and arterial blood). Since an anesthetic's concentration in the brain tissue is directly proportional to its partial pressure, it is possible to use the steady-state alveolar partial pressure of the inhaled agent as a measure of anesthetic potency.

The minimal alveolar concentration (MAC) refers to the percentage of anesthetic in the inspired gas mixture that renders 50% of patients unresponsive to painful stimuli. It corresponds to $ED_{50}$ on the dose-effect curve. Potency is inversely proportional to the MAC: the lower the MAC, the more potent the anesthetic. MAC is an intrinsic property of the anesthetic that does not depend on the type of surgery; duration of anesthesia; or the sex, height, and weight of the patient. It does, however, depend on body temperature and also decreases with increasing patient age.

**(Choice A)** The arteriovenous concentration gradient is an indirect measurement of the solubility of the anesthetic in body tissues. A high arteriovenous concentration gradient means that more anesthetic is extracted from the blood by the body tissues, increasing the time it takes for the blood to become saturated and slowing the onset of action.


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**(Choice B)** The blood/gas partition coefficient corresponds to the solubility of anesthetic in the blood. Anesthetics with a high blood/gas partition coefficient are absorbed to a greater extent by the blood and have a slower onset of action.

**(Choice C)** Clearance of inhaled anesthetics occurs mainly via exhalation from the lungs into the air; hepatic metabolism of most gas anesthetics is low. However, certain gas anesthetics, particularly halothane, are metabolized extensively by the liver, resulting in the production of reactive intermediates that cause hepatotoxicity.

**(Choice E)** The steepness of the arterial tension curve depends on the solubility of the anesthetic in the blood. Partial pressure in the blood rises more rapidly with less soluble anesthetics, producing a steeper curve.

**Educational objective:**
The minimal alveolar concentration (MAC) is a measure of potency of an inhaled anesthetic. It is the concentration of the anesthetic in the alveoli that renders 50% of patients unresponsive to painful stimuli ($ED_{50}$). Potency is inversely proportional to the MAC: the lower the MAC, the more potent the anesthetic.

Pharmacology Nervous System Efficacy and potency


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A 29-year-old woman comes to the office for treatment of anxiety that has worsened over the past year. She finds herself worrying all the time and fears that she may not complete her graduate studies in time to meet requirements for her degree. The patient is also worried about her son's health and anxiously obsesses about him all the time. She says, "My anxiety just comes out of the blue; one way or another, I'm anxious all the time." The patient has no history of medical problems. Physical examination is unremarkable; complete blood count, chemistry panel, and TSH and $B_{12}$ levels are normal. An anxiety disorder is diagnosed and fluoxetine is prescribed. The patient's anxiety begins to improve over the next 4-6 weeks. The physician explains that the medication inhibits the reuptake of a neurotransmitter released by a specific set of neurons. These neurons are most likely part of which of the following structures?

A. Caudate nucleus
B. Locus ceruleus
C. Nucleus basalis of Meynert
D. Raphe nuclei
E. Red nucleus


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She finds herself worrying all the time and fears that she may not complete her graduate studies in time to meet requirements for her degree. The patient is also worried about her son's health and anxiously obsesses about him all the time. She says, "My anxiety just comes out of the blue; one way or another, I'm anxious all the time." The patient has no history of medical problems. Physical examination is unremarkable; complete blood count, chemistry panel, and TSH and $B_{12}$ levels are normal. An anxiety disorder is diagnosed and fluoxetine is prescribed. The patient's anxiety begins to improve over the next 4-6 weeks. The physician explains that the medication inhibits the reuptake of a neurotransmitter released by a specific set of neurons. These neurons are most likely part of which of the following structures?

A. Caudate nucleus
B. Locus ceruleus
C. Nucleus basalis of Meynert
D. Raphe nuclei
E. Red nucleus
F. Substantia nigra



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obsesses about him all the time. She says, "My anxiety just comes out of the blue; one way or another, I'm anxious all the time." The patient has no history of medical problems. Physical examination is unremarkable; complete blood count, chemistry panel, and TSH and $B_{12}$ levels are normal. An anxiety disorder is diagnosed and fluoxetine is prescribed. The patient's anxiety begins to improve over the next 4-6 weeks. The physician explains that the medication inhibits the reuptake of a neurotransmitter released by a specific set of neurons. These neurons are most likely part of which of the following structures?

- A. Caudate nucleus (5%)
- B. Locus ceruleus (20%)
- C. Nucleus basalis of Meynert (6%)
- ✓ D. Raphe nuclei (61%)
- E. Red nucleus (1%)
- F. Substantia nigra (3%)

Correct

61%
Answered correctly

55 secs
Time Spent

01/08/2021
Last Updated



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In the **central nervous system (CNS), serotonergic** (serotonin-releasing) **neurons** are primarily found in the **raphe nuclei** of the brainstem. The raphe nuclei are located in the midbrain, pons, and medulla, and axons from these cell bodies project widely throughout the CNS to synapse on structures such as the cerebral cortex, thalamus, hypothalamus, cerebellum, hippocampus, and spinal cord. These neurons play a role in the sleep-wake cycle, anxiety, mood, psychosis, sexuality, eating behavior, and impulsivity.

Medications that target serotonin neurons are widely used in psychiatric disorders. Serotonergic antidepressants are the primary pharmacotherapy for most depressive and anxiety disorders. Antidepressants such as selective serotonin reuptake inhibitors (SSRIs [eg, fluoxetine]), serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressants work by prolonging the amount of time that serotonin spends in the synaptic clefts of these neurons before being taken up by presynaptic neurons.

**(Choice A)** The caudate nucleus and putamen form the striatum, which functions in motor activities. In Huntington disease, there is loss of cholinergic and GABA-releasing neurons in the striatum.

**(Choice B)** The locus ceruleus houses norepinephrine-secreting neurons that participate in activation of the "fight or flight" response to physical and emotional stressors. It is located in the dorsal pons. These neurons are implicated in some anxiety symptoms, but they are not serotonergic and not affected by SSRIs.


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the "fight or flight" response to physical and emotional stressors. It is located in the dorsal pons. These neurons are implicated in some anxiety symptoms, but they are not serotonergic and not affected by SSRIs.

**(Choice C)** The nucleus basalis of Meynert houses the cell bodies of cholinergic neurons. In Alzheimer disease, these neurons secrete decreased amounts of acetylcholine.

**(Choice E)** The red nucleus is located in the anterior midbrain. Its neurons participate in motor coordination of the upper extremities.

**(Choice F)** The substantia nigra contains dopaminergic neurons. In Parkinson disease, these neurons are depleted.

**Educational objective:**
Serotonin-releasing neurons in the central nervous system (CNS) are located in the raphe nuclei. These neurons disseminate widely to synapse on numerous structures in the CNS. Antidepressants such as selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressants inhibit serotonin reuptake at these synapses.

**References**

- Stress-related serotonergic systems: implications of symptomatology of anxiety and affectivedisorders.


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A 5-year-old boy is brought to the emergency department due to recurrent, generalized tonic-clonic seizures over the past 24 hours. The patient has been having high fever and flulike symptoms for the past 3 days. He has a past medical history of febrile seizures at age 6 months. He takes no medications and has no family history of epilepsy. The patient's temperature is 39.4 C (103 F), blood pressure is 110/70 mm Hg, pulse is 112/min, and respirations are 10/min. He appears lethargic and does not follow simple commands consistently. His neck is supple. During the examination, the patient suddenly develops sustained, generalized tonic-clonic convulsions without fully regaining consciousness between episodes. Which of the following describes the mechanism of action of the most appropriate initial therapy for his seizures?

A. Blockade of presynaptic voltage-gated calcium channels
B. Blockade of presynaptic voltage-gated sodium channels
C. Enhanced postsynaptic chloride influx
D. Inhibition of presynaptic neurotransmitter reuptake
E. Inhibition of vesicle fusion and neurotransmitter release


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3 days. He has a past medical history of febrile seizures at age 6 months. He takes no medications and has no family history of epilepsy. The patient's temperature is 39.4 C (103 F), blood pressure is 110/70 mm Hg, pulse is 112/min, and respirations are 10/min. He appears lethargic and does not follow simple commands consistently. His neck is supple. During the examination, the patient suddenly develops sustained, generalized tonic-clonic convulsions without fully regaining consciousness between episodes. Which of the following describes the mechanism of action of the most appropriate initial therapy for his seizures?

A. Blockade of presynaptic voltage-gated calcium channels (8%)
B. Blockade of presynaptic voltage-gated sodium channels (38%)
C. Enhanced postsynaptic chloride influx (48%)
D. Inhibition of presynaptic neurotransmitter reuptake (2%)
E. Inhibition of vesicle fusion and neurotransmitter release (2%)

Correct
48%
02 mins, 14 secs
03/12/2021


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This patient has **status epilepticus**, possibly due to complex febrile seizures or infectious meningitis/encephalitis. Regardless of etiology, the initial drug of choice for treating status epilepticus is an **intravenous benzodiazepine** (eg, lorazepam), due to its efficacy and rapid onset of action.

Benzodiazepines enhance the effect of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) at the **GABA-A receptor**, a ligand-gated ion channel. Allosteric attachment of benzodiazepines to the GABA-A receptor causes increased **influx** of negatively charged **chloride ions** in response to GABA binding. This leads to hyperpolarization of the postsynaptic neuron and suppression of action potential firing (anticonvulsant effect).

**(Choices A and E)** Presynaptic voltage-gated calcium channels mediate the influx of calcium into the axon terminal, promoting vesicle fusion and neurotransmitter release into the synaptic cleft. Gabapentin is an anticonvulsant that works by blocking voltage-gated calcium channels, thereby attenuating excitatory neurotransmitter release.

**(Choice B)** Presynaptic voltage-gated sodium channels open when the cell becomes sufficiently depolarized, triggering an action potential that propagates down the axon. Phenytoin blocks presynaptic voltage-gated sodium channels and can be used to prevent recurrence of status epilepticus due to its long duration of action. However, it has a slow onset of action, and patients in status epilepticus should be


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depolarized, triggering an action potential that propagates down the axon. Phenytoin blocks presynaptic voltage-gated sodium channels and can be used to prevent recurrence of status epilepticus due to its long duration of action. However, it has a slow onset of action, and patients in status epilepticus should be given a rapid-acting benzodiazepine first.

**(Choice D)** Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are examples of medications that prevent presynaptic neurotransmitter reuptake. They are typically used to treat depression and anxiety disorders.

**Educational objective:**

Intravenous benzodiazepines (eg, lorazepam) are the initial drug of choice for status epilepticus. They work by enhancing the effect of gamma-aminobutyric acid (GABA) at the GABA-A receptor, leading to increased chloride influx and suppression of action potential firing.

**References**

- Benzodiazepine pharmacology and central nervous system-mediated effects.
- Pharmacotherapy for Status Epilepticus.

Pharmacology  Nervous System  Seizures



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A 54-year-old man is brought to the emergency department due to acute onset mental status change and double vision. On examination, he is disoriented to time and place and has a decreased attention span. Further questioning reveals memory impairment that appears to be most severe during the last several years. Neurologic examination shows horizontal nystagmus evoked on lateral gaze with bilateral weakness of the lateral rectus muscles. The patient is unable to stand without external support. Thiamine infusion is started immediately, and his condition improves significantly over the next several days. Which of the following neurologic findings is most likely to persist despite treatment?

A. Ataxia
B. Disorientation
C. Inattention
D. Memory loss
E. Ophthalmopathy

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A 54-year-old man is brought to the emergency department due to acute onset mental status change and double vision. On examination, he is disoriented to time and place and has a decreased attention span. Further questioning reveals memory impairment that appears to be most severe during the last several years. Neurologic examination shows horizontal nystagmus evoked on lateral gaze with bilateral weakness of the lateral rectus muscles. The patient is unable to stand without external support. Thiamine infusion is started immediately, and his condition improves significantly over the next several days. Which of the following neurologic findings is most likely to persist despite treatment?

A. Ataxia (6%)
B. Disorientation (0%)
C. Inattention (1%)
✓ D. Memory loss (82%)
E. Ophthalmopathy (8%)

82%
35 secs
10/18/2020



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| Features of Wernicke-Korsakoff syndrome | |
|---|---|
| **Associated conditions** | • Chronic **alcoholism** (most common)<br>• Malnutrition |
| **Pathophysiology** | • **Thiamine deficiency** → impairs ATP generation → neuronal dysfunction/death<br>• Paraventricular lesions (eg, **mammillary bodies**, dorsomedial thalamus) |
| **Clinical findings** | • **Confusion**<br>• **Oculomotor dysfunction** (eg, horizontal nystagmus & bilateral abducens palsy)<br>• Postural & gait **ataxia**<br>• Memory impairment (permanent) |
| **Treatment** | • Intravenous thiamine<br>• Administration of glucose before thiamine can worsen symptoms |

The characteristic manifestations of Wernicke syndrome, a condition caused by chronic thiamine (vitamin


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The characteristic manifestations of Wernicke syndrome, a condition caused by chronic thiamine (vitamin $B_1$) deficiency, are as follows:

- **Oculomotor dysfunction**: Occurs due to damage involving the oculomotor nerve (CN III), abducens nerve (CN VI), and vestibular nuclei. It is rapidly reversible and usually resolves almost completely with thiamine administration **(Choice E)**.
- **Ataxia**: Caused by damage to the cerebellar cortex and vestibular nuclei. Unlike oculomotor function, ataxia takes longer to resolve and some patients may have permanent symptoms **(Choice A)**.
- **Mental status changes**: Disorientation, apathy, and decreased attention span respond well to treatment **(Choices B and C)**. However, memory and learning abnormalities usually persist as a condition known as Korsakoff syndrome.

Korsakoff syndrome is associated with damage to the **anterior and dorsomedial thalamic nuclei**. This results in memory loss and a psychological phenomenon called "confabulation." When patients with Korsakoff syndrome are unsure of a fact, they fill in the memory gap with a fabricated story that they themselves believe to be true. Korsakoff syndrome also results in an inability to form new memories (anterograde amnesia). These impairments in memory and learning are usually permanent.

Thiamine should be administered immediately in all patients with suspected Wernicke encephalopathy


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Thiamine should be administered immediately in all patients with suspected Wernicke encephalopathy because it can help limit irreversible neurologic damage.

**Educational objective:**

Oculomotor dysfunction, ataxia, and confusion form the triad of Wernicke syndrome. Most of these symptoms usually resolve after thiamine administration. Korsakoff syndrome is a complication of Wernicke encephalopathy, the hallmarks of which are permanent memory loss and confabulation.

**References**

- Wernicke-Korsakoff syndrome.

| Pathology | Nervous System | Wernicke korsakoff syndrome |
|---|---|---|
| Subject | System | Topic |



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A 60-year-old man comes to the office due to difficulties in tasting food. He says, "All food now tastes bland," and he is unable to enjoy different flavors during meals. Two months ago, the patient had a traumatic brain injury after a head-on motor vehicle collision. He was in a coma for several days and, after regaining consciousness, began having severe headaches and impaired taste. The headaches have improved, but he continues to have difficulty tasting food. The patient has no visual concerns, slurred speech, trouble swallowing, vertigo, or extremity weakness or numbness. He is a truck driver and has a history of heavy tobacco use for many years. Vital signs are within normal limits. Physical examination shows no focal motor deficits. Which of the following is the most likely cause of this patient's current symptoms?

A. Anterior temporal lobe contusion
B. Avulsion of olfactory nerve rootlets
C. Ischemic stroke of the dorsolateral medulla
D. Lingual nerve injury
E. Sphenoid bone fracture



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bland," and he is unable to enjoy different flavors during meals. Two months ago, the patient had a traumatic brain injury after a head-on motor vehicle collision. He was in a coma for several days and, after regaining consciousness, began having severe headaches and impaired taste. The headaches have improved, but he continues to have difficulty tasting food. The patient has no visual concerns, slurred speech, trouble swallowing, vertigo, or extremity weakness or numbness. He is a truck driver and has a history of heavy tobacco use for many years. Vital signs are within normal limits. Physical examination shows no focal motor deficits. Which of the following is the most likely cause of this patient's current symptoms?

A. Anterior temporal lobe contusion (6%)
B. Avulsion of olfactory nerve rootlets (69%)
C. Ischemic stroke of the dorsolateral medulla (4%)
D. Lingual nerve injury (9%)
E. Sphenoid bone fracture (8%)

69%
01 min, 51 secs
10/15/2020


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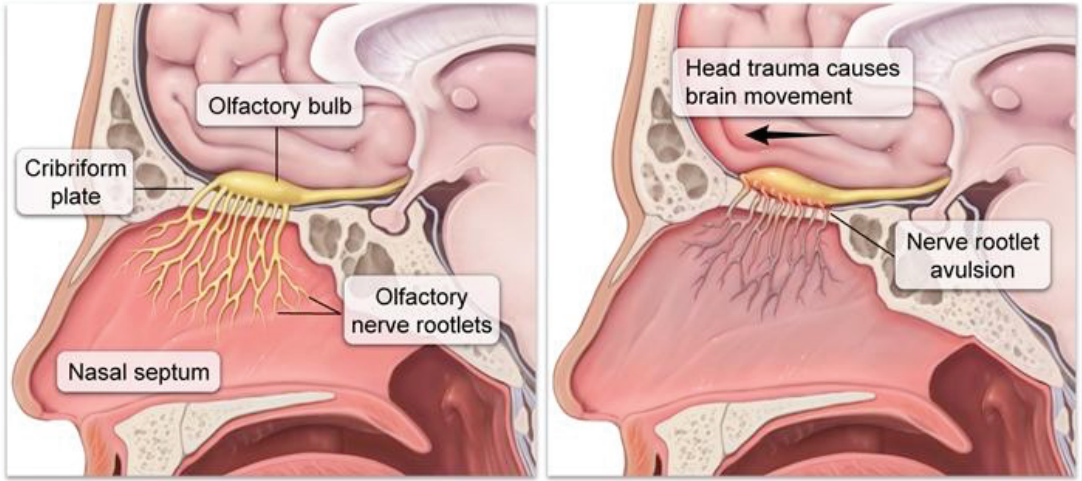
**Olfactory nerve rootlet avulsion with TBI**




**TBI** = traumatic brain injury.
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This patient has a decreased perception of flavors after **traumatic brain injury**. The perception of flavor is dependent on both smell and taste, with smell being more important. Patients with **anosmia (loss of smell)** often describe difficulties with taste, even if taste sensation is intact.


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**TBI** = traumatic brain injury.
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This patient has a decreased perception of flavors after **traumatic brain injury**. The perception of flavor is dependent on both smell and taste, with smell being more important. Patients with **anosmia (loss of smell)** often describe difficulties with taste, even if taste sensation is intact.

The perception of smell is mediated by odorant molecules that bind to olfactory chemoreceptor cells in the nasal mucosa. Axons of the chemoreceptor cells make up the olfactory nerve (CN I) rootlets, which project through the **cribriform plate** of the ethmoid bone to synapse on the glomeruli of the olfactory bulb. The olfactory bulb then projects second-order axons to the primary olfactory cortex in the medial temporal lobe via the olfactory tract.

Head trauma can cause anosmia when acceleration-deceleration forces lead to **avulsion** of the **olfactory nerve rootlets** as they transverse the cribriform plate.

**(Choice A)** The anterior temporal lobe is important for semantic memory; as a result, injury to this brain region typically results in impaired comprehension about the meaning of words, pictures, and objects.

**(Choice C)** Dorsolateral medulla infarction causes Wallenberg syndrome. This condition is characterized by vertigo/nystagmus, ipsilateral cerebellar signs (eg, ataxia, dysmetria), loss of pain/temperature


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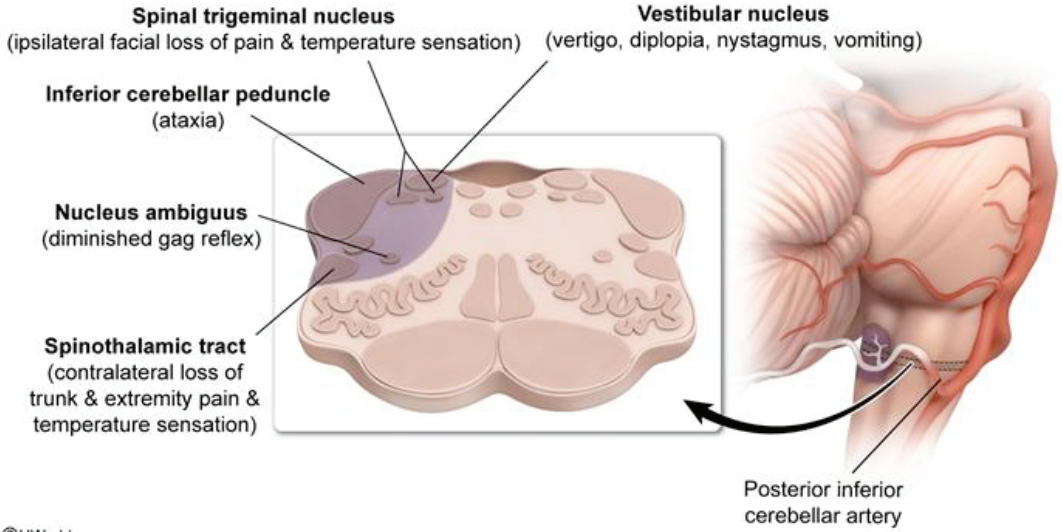
Exhibit Display

## Lateral medullary (Wallenberg) syndrome

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**(Choice C)** Dorsolateral medulla infarction causes Wallenberg syndrome. This condition is characterized by vertigo/nystagmus, ipsilateral cerebellar signs (eg, ataxia, dysmetria), loss of pain/temperature sensation in the ipsilateral face and contralateral body, bulbar weakness (eg, dysphagia), and ipsilateral Horner syndrome (miosis, ptosis, anhidrosis).

**(Choice D)** The lingual nerve is a branch of the mandibular division of the trigeminal nerve (CN V3) that provides somatic sensation to the anterior two-thirds of the tongue. Fibers of the chorda tympani nerve, a branch of the facial nerve (CN VII), also travel with the lingual nerve to relay taste from the anterior two-thirds of the tongue. If taste disturbances were due to injury of the lingual nerve, tongue numbness would also be present.

**(Choice E)** Sphenoid bone fractures are associated with damage to the optic nerve (CN II), pituitary gland injury, and leakage of cerebrospinal fluid into the sphenoid sinus.

**Educational objective:**
Olfactory signals are relayed via the olfactory nerve (CN I) through the cribriform plate to the olfactory bulb, which then projects to the primary olfactory cortex in the medial temporal lobe. Head trauma can tear olfactory nerve (CNI) rootlets as they cross the cribriform plate, causing anosmia. Anosmia is often interpreted by patients as loss of taste.


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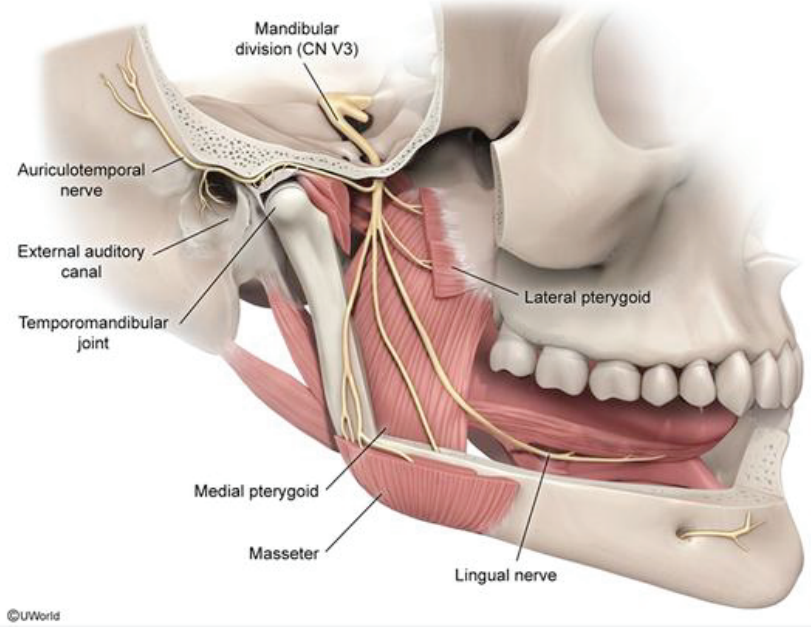
Mandibular division of trigeminal nerve

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interpreted by patients as loss of taste.



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A 72-year-old woman comes to the office for a routine follow-up visit accompanied by her son. The patient has experienced progressive memory loss over the last 2 years. She now needs help with her daily activities, such as shopping and housekeeping. The patient's son says, "She used to be such an independent person, but now she needs help with most things. She even forgot my name the other day!" Medical history includes hypertension, hyperlipidemia, and type 2 diabetes mellitus. Family history includes major depressive disorder in her father. MRI reveals diffuse cortical and hippocampal atrophy. Which of the following biochemical changes is most likely contributing to this patient's condition?

A. Decreased choline acetyltransferase activity in the nucleus basalis
B. Decreased dopa decarboxylase activity in the substantia nigra
C. Decreased tryptophan hydroxylase activity in the raphe nuclei
D. Increased acetylcholinesterase activity in the caudate nucleus
E. Increased dopamine beta-hydroxylase activity in the locus ceruleus

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A 72-year-old woman comes to the office for a routine follow-up visit accompanied by her son. The patient has experienced progressive memory loss over the last 2 years. She now needs help with her daily activities, such as shopping and housekeeping. The patient's son says, "She used to be such an independent person, but now she needs help with most things. She even forgot my name the other day!" Medical history includes hypertension, hyperlipidemia, and type 2 diabetes mellitus. Family history includes major depressive disorder in her father. MRI reveals diffuse cortical and hippocampal atrophy. Which of the following biochemical changes is most likely contributing to this patient's condition?

A. Decreased choline acetyltransferase activity in the nucleus basalis (67%)

B. ~~Decreased dopa decarboxylase activity in the substantia nigra~~ (6%)

C. ~~Decreased tryptophan hydroxylase activity in the raphe nuclei~~ (6%)

D. ~~Increased acetylcholinesterase activity in the caudate nucleus~~ (17%)

E. ~~Increased dopamine beta-hydroxylase activity in the locus ceruleus~~ (3%)

67% 02 mins 01 sec 02/06/2021



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| Clinical features of Alzheimer disease | |
|---|---|
| **Early findings** | • Anterograde memory loss (ie, immediate recall affected, distant memories preserved)<br>• Visuospatial deficits (eg, lost in own neighborhood)<br>• Language difficulties (eg, difficulty finding words)<br>• Cognitive impairment with progressive decline |
| **Late findings** | • Neuropsychiatric (eg, hallucinations, wandering)<br>• Dyspraxia (eg, difficulty performing learned motor tasks)<br>• Lack of insight regarding deficits<br>• Noncognitive neurologic deficits (eg, pyramidal & extrapyramidal motor, myoclonus, seizures)<br>• Urinary incontinence |

Alzheimer disease (AD) is the most common cause of dementia. It has the following characteristic features:

- Prevailing clinical symptom: slow, progressive memory loss



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features:

- Prevailing clinical symptom: slow, progressive memory loss
- Macroscopic brain appearance: mild-to-moderate generalized brain atrophy
- Microscopic brain changes: neurofibrillary tangles, senile plaques, and amyloid angiopathy
- Biochemical abnormalities: decreased acetylcholine levels in the hippocampus and nucleus basalis of Meynert

The most important biochemical abnormality noted in AD is a **decrease** in the **acetylcholine level**. This occurs due to a **deficiency** of **choline acetyltransferase**. The decline in acetylcholine is most notable in the **nucleus basalis of Meynert**, which participates in memory and cognition. This nucleus is located at the base of the forebrain and widely projects to the neocortex. Another involved structure is the **hippocampus**: The major function of the hippocampus is the formation of new memories.

Symptomatic management of AD includes cholinesterase inhibitors, which target the acetylcholine deficit by inhibiting the degradation of acetylcholine at the synaptic cleft.

**(Choice B)** Loss of dopaminergic neurons in the substantia nigra is seen in Parkinson disease and dementia with Lewy bodies.



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**(Choice C)** The raphe nuclei form the medial part of the brain stem's reticular formation (medulla, pons, and midbrain). Many neurons in the nuclei are serotonergic. Serotonin is implicated in the pathogenesis of anorexia, depression, and sleep disorders.

**(Choice D)** Atrophy of the caudate nucleus is seen in Huntington disease.

**(Choice E)** The locus ceruleus is thought to play a role in the pathogenesis of panic attacks and panic disorder. It is located in the pons and contains cell bodies of noradrenergic neurons that synthesize norepinephrine.

**Educational objective:**

Alzheimer disease is characterized by decreased levels of acetylcholine in the nucleus basalis of Meynert and the hippocampus, caused by diminished activity of choline acetyltransferase.

**References**

- Alzheimer's disease: targeting the cholinergic system.

| Pathology | Nervous System | Alzheimer disease |
|---|---|---|
| Subject | System | Topic |

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A 16-year-old boy is being evaluated for difficulty walking. On physical examination, he has thoracic scoliosis and multiple small scars on his hands. When asked about these, the boy replies, "I frequently burn my hands by accident because I can't feel the heat." Neurologic examination reveals 1+ biceps reflexes and 3+ patellar reflexes bilaterally, as well as decreased muscle strength in the bilateral upper and lower extremities. His hand muscles are atrophic, and position and vibration senses in the feet are also impaired. Which of the following is the most likely cause of this patient's problems?

A. Amyotrophic lateral sclerosis
B. Guillain-Barré syndrome
C. Medulloblastoma
D. Multiple sclerosis
E. Normal pressure hydrocephalus
F. Syringomyelia

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- A. Amyotrophic lateral sclerosis (23%)
- B. ~~Guillain-Barré syndrome~~ (5%)
- C. Medulloblastoma (5%)
- D. ~~Multiple sclerosis~~ (4%)
- E. ~~Normal pressure hydrocephalus~~ (0%)
- F. Syringomyelia (60%)



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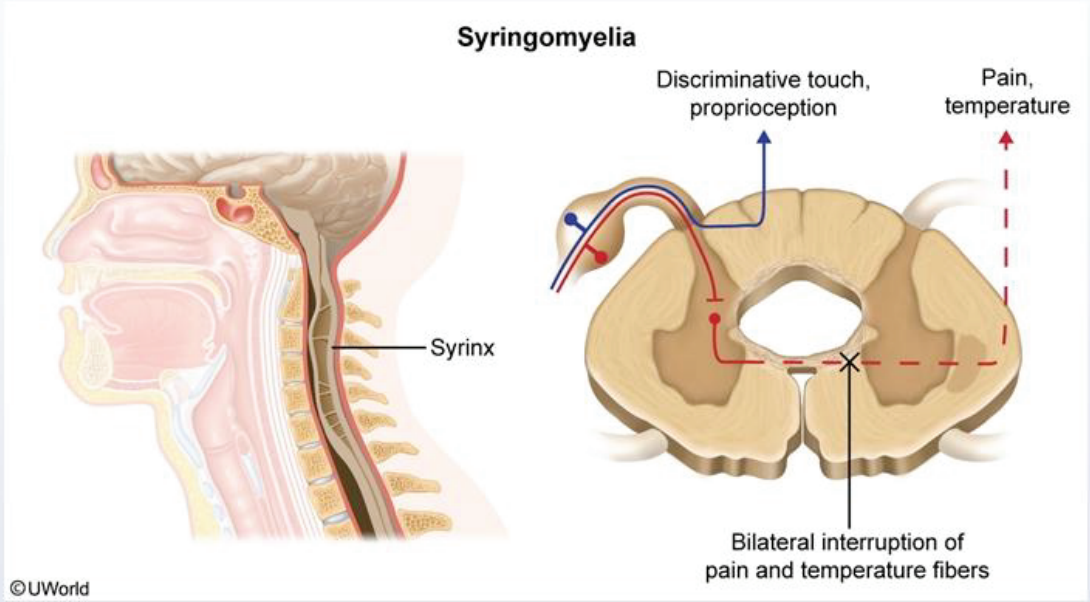


This patient has chronic **loss of upper extremity pain and temperature sensations**, upper extremity weakness and hyporeflexia, lower extremity weakness and hyperreflexia, and kyphoscoliosis. These findings are consistent with **syringomyelia**.


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findings are consistent with **syringomyelia**.

In syringomyelia, a **central cystic dilation** in the cervical spinal cord (a syrinx) slowly enlarges, characteristically causing damage to the **ventral white commissure** and **anterior horns**. The ventral white commissure is the site of decussation of second-order lateral spinothalamic tract neurons, and the ventral horns are the site of lower motor neuron cell bodies. The syrinx is most commonly situated at the C8-T1 cord levels and may extend rostrally, caudally, and centrifugally. Further expansion within the cervical cord in later stages of the disease can produce lower extremity weakness and hyperreflexia (an upper motor neuron defect) by affecting the lateral corticospinal tract and can also lead to loss of position and vibration senses in the feet due to involvement of the posterior columns. Scoliosis can occur due to paresis of paravertebral muscles.

**(Choice A)** Amyotrophic lateral sclerosis is a progressive degenerative disease of upper and lower motor neurons only; it does not cause sensory loss.

**(Choice B)** Guillain-Barré syndrome is a peripheral nervous system autoimmune demyelinating polyneuropathy that typically causes lower motor neuron manifestations (eg, areflexia, weakness) in a symmetric ascending pattern.

**(Choice C)** Medulloblastoma is the most common malignant central nervous system (CNS) tumor in children, with pilocytic astrocytoma, a low-grade astrocytoma, being the most common CNS tumor overall


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**(Choice B)** Guillain-Barré syndrome is a peripheral nervous system autoimmune demyelinating polyneuropathy that typically causes lower motor neuron manifestations (eg, areflexia, weakness) in a symmetric ascending pattern.

**(Choice C)** Medulloblastoma is the most common malignant central nervous system (CNS) tumor in children, with pilocytic astrocytoma, a low-grade astrocytoma, being the most common CNS tumor overall. Medulloblastoma is a posterior fossa tumor that causes symptoms related to obstructive hydrocephalus.

**(Choice D)** Multiple sclerosis is an autoimmune CNS demyelinating disorder that presents with episodic neurologic symptoms reflecting defects in various white matter tracts.

**(Choice E)** Normal pressure hydrocephalus is characterized by gait ataxia and urinary incontinence. It is rare in patients age <60. Defective cerebrospinal fluid resorption by the arachnoid granulations gives rise to the secondary form of this disease.

**Educational objective:**
The combination of fixed segmental loss of upper extremity pain and temperature sensations, upper extremity lower motor neuron signs, and/or lower extremity upper motor neuron signs in the setting of scoliosis suggests syringomyelia.



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A 54-year-old previously healthy man comes to the office due to progressive fatigue and weakness for the past 2 months. His weakness predominantly involves the lower extremities, causing him to have difficulty rising from a chair. The patient also has a persistent cough and unintentional 7-kg (15.4-lb) weight loss during the same period. He has a 30-pack-year smoking history and drinks alcohol occasionally. Physical examination shows bilaterally decreased strength in the proximal muscles of the lower extremities with normal bulk and tone. Quadriceps tendon reflexes are diminished bilaterally. Chest x-ray reveals a hilar mass, biopsy of which demonstrates small cells that stain positive for chromogranin and synaptophysin. Which of the following is the most likely cause of this patient's muscle weakness?

A. Antibodies against voltage-gated calcium channels
B. Antibodies against nicotinic acetylcholine receptors
C. Immune-mediated, segmental axonal demyelination
D. Neoplastic deposits in the spinal cord epidural space
E. Ubiquitin-proteasome-mediated muscle protein degradation


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- A. Antibodies against voltage-gated calcium channels (77%)
- B. Antibodies against nicotinic acetylcholine receptors (8%)
- C. Immune-mediated, segmental axonal demyelination (4%)
- D. Neoplastic deposits in the spinal cord epidural space (8%)
- E. Ubiquitin-proteasome-mediated muscle protein degradation (2%)

Correct

77%
Answered correctly

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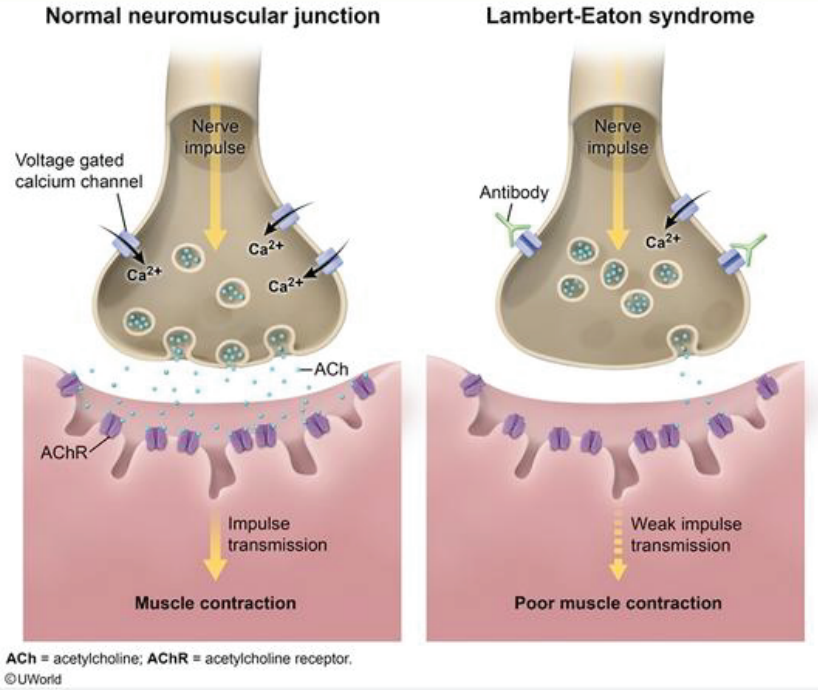


**ACh** = acetylcholine; **AChR** = acetylcholine receptor.

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This patient with small cell lung cancer (small cells with neuroendocrine differentiation) has progressive proximal muscle weakness and diminished reflexes in the lower extremities, suggestive of paraneoplastic **Lambert-Eaton myasthenic syndrome** (LEMS). LEMS is an autoimmune disorder characterized by **antibodies against presynaptic voltage-gated calcium channels** at the neuromuscular junction. Normally, these calcium channels open in response to a presynaptic action potential, leading to an influx of calcium ions that cause synaptic vesicle fusion and acetylcholine release. LEMS-associated autoantibodies inhibit calcium influx, resulting in reduced acetylcholine release and failure to provoke muscular contractions.

Muscular weakness in LEMS is progressive and predominantly involves the **proximal muscles**; it typically affects the **lower limbs** (eg, difficulty rising from a chair or climbing stairs) before the upper limbs (eg, raising arms above the head). **Deep tendon reflexes** are typically **diminished** or absent. Both strength and reflexes improve transiently with isometric muscular contractions in a phenomenon known as **postexercise facilitation**, likely due to a buildup of intracellular calcium with repetitive stimuli. Approximately 50% of patients have an underlying malignancy, most commonly **small cell lung cancer**.

**(Choice B)** Autoantibodies against postsynaptic nicotinic acetylcholine receptors cause myasthenia gravis (MG), another immune-mediated neuromuscular disorder. MG typically involves the extraocular (eg, ptosis,



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Approximately 50% of patients have an underlying malignancy, most commonly **small cell lung cancer**.

**(Choice B)** Autoantibodies against postsynaptic nicotinic acetylcholine receptors cause myasthenia gravis (MG), another immune-mediated neuromuscular disorder. MG typically involves the extraocular (eg, ptosis, diplopia) and bulbar (eg, dysphonia, dysphagia) muscles before affecting the limbs, and reflexes typically remain intact.

**(Choice C)** Guillain-Barré syndrome occurs due to immune-mediated, segmental axonal demyelination; however, it typically occurs after an upper respiratory or gastrointestinal (eg, *Campylobacter*) infection. Rapidly progressive ascending paralysis (distal prior to proximal muscle involvement) is characteristic.

**(Choice D)** Metastatic disease within the epidural space can cause spinal cord compression. Patients typically develop spastic paraparesis below the level of involvement. Hyperreflexia is common, and urine and stool retention may be seen (depending on the level of involvement).

**(Choice E)** Protein degradation in cancer cachexia is associated with activation of the ubiquitin-proteasome system. Cancer cachexia causes muscle and fat loss, but weakness would be expected to affect proximal and distal muscles equally and reflexes are preserved.

**Educational objective:**

Lambert-Eaton myasthenic syndrome is characterized by antibodies against presynaptic voltage-gated



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Approximately 50%

**(Choice B)** Autoar

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**(Choice C)** Guillai

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**(Choice D)** Metast

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**(Choice E)** Protein

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| Autoimmune-mediated neuromuscular junction disorders | | |
|---|---|---|
| | **Myasthenia gravis** | **Lambert-Eaton myasthenic syndrome** |
| **Antibodies** | Acetylcholine receptor antibody | Voltage-gated calcium channel antibody |
| **Location of defect** | Postsynaptic | Presynaptic |
| **Weakness** | Extraocular & bulbar affected first (eg, ptosis, diplopia) | Proximal muscles affected first (eg, weakness standing from chair) |
| **Deep-tendon reflexes** | Intact | Decreased/absent |
| **Autonomic dysfunction** | Rare | Common |
| **Association** | Thymoma/thymic hyperplasia | Malignancy (eg, small cell lung cancer) |
| **Tensilon test (edrophonium)** | Improves weakness | No change |
| **Response to exercise** | Decreased strength | Increased strength |
| **Nerve stimulation** | | |

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Approximately 50%

**(Choice B)** Autoar
(MG), another imm
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**(Choice C)** Guillai
however, it typically
Rapidly progressive

**(Choice D)** Metast
typically develop sp
and stool retention

**(Choice E)** Protein
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| | Myasthenia gravis | Lambert-Eaton myasthenic syndrome |
|---|---|---|
| **Antibodies** | Acetylcholine receptor antibody | Voltage-gated calcium channel antibody |
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| **Tensilon test (edrophonium)** | Improves weakness | No change |
| **Response to exercise** | Decreased strength | Increased strength |
| **Nerve stimulation studies** | Decremental response | Incremental response |

New | Existing



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however, it typically occurs after an upper respiratory or gastrointestinal (eg, *Campylobacter*) infection. Rapidly progressive ascending paralysis (distal prior to proximal muscle involvement) is characteristic.

**(Choice D)** Metastatic disease within the epidural space can cause spinal cord compression. Patients typically develop spastic paraparesis below the level of involvement. Hyperreflexia is common, and urine and stool retention may be seen (depending on the level of involvement).

**(Choice E)** Protein degradation in cancer cachexia is associated with activation of the ubiquitin-proteasome system. Cancer cachexia causes muscle and fat loss, but weakness would be expected to affect proximal and distal muscles equally and reflexes are preserved.

**Educational objective:**
Lambert-Eaton myasthenic syndrome is characterized by antibodies against presynaptic voltage-gated calcium channels. Patients develop progressive proximal muscle weakness with reduced/absent reflexes that predominantly involves the lower extremities. The syndrome is often associated with malignancy, particularly small cell lung cancer.

| Pathology | Nervous System | Eaton lambert myasthenic syndrome |
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| Subject | System | Topic |



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A 64-year-old woman is evaluated for episodic urinary incontinence. Urodynamic studies reveal an overactive bladder. Symptoms persist after behavioral interventions, and the patient is unable to tolerate medical treatment. Low-amplitude electrical stimulation therapy that helps modulate neural control of the urinary bladder muscle, urethral sphincter, and pelvic muscles is planned. A stimulating electrode is most likely to be placed close to which of the following structures during this procedure?

A. Nucleus accumbens
B. Subthalamic nucleus
C. Vagus nerve
D. T6 nerve root
E. L5 nerve root
F. S3 nerve root

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A. ~~Nucleus accumbens~~ (2%)
B. ~~Subthalamic nucleus~~ (2%)
C. ~~Vagus nerve~~ (6%)
D. ~~T6 nerve root~~ (3%)
E. ~~L5 nerve root~~ (19%)
F. S3 nerve root (65%)

Correct

65%
Answered correctly

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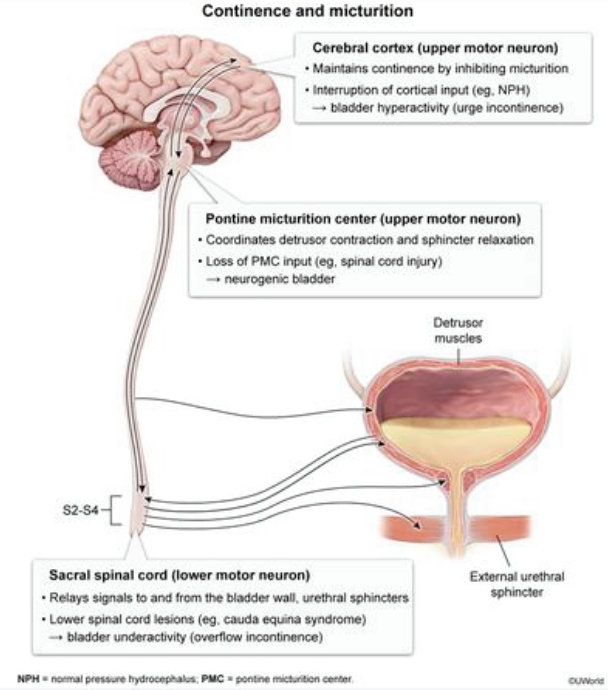


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**NPH** = normal pressure hydrocephalus; **PMC** = pontine micturition center. ©UWorld

This patient has urge incontinence due to an overactive bladder. In patients unresponsive to behavioral therapy and unable to take medications, a bladder stimulator is sometimes used. Neural stimulation is used to augment neural signals to the pelvic floor muscles and urinary sphincter, which are innervated from nerves derived from the **S2-S4 nerve roots**:

- **Somatic innervation** of the **pelvic floor muscles** helps to maintain continence because these muscles stabilize the urethra against the anterior vaginal wall. This contraction decreases the angle between the bladder neck and the urethra (ie, urethrovesical angle), thereby compressing the urethra, stopping urine flow, and maintaining continence. Therefore, increasing the strength of the pelvic floor muscles (either through physical therapy or neuromodulatory stimulation) promotes continence.
- The **external urethral sphincter** (EUS) is also under somatic control via the **pudendal nerve** (S2-S4); therefore, stimulation of these nerve roots will increase EUS tone to help improve urinary continence.

Although the **pelvic splanchnic nerves**, derived from S2-S4, are classically described as providing **parasympathetic** input to the bladder and urethral sphincter (which promotes bladder contraction and may worsen incontinence), they are also involved in the **bladder stretch-contraction reflex**. Neural stimulation seems to inhibit this reflex to improve continence.



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**parasympathetic** input to the bladder and urethral sphincter (which promotes bladder contraction and may worsen incontinence), they are also involved in the **bladder stretch-contraction reflex**. Neural stimulation seems to inhibit this reflex to improve continence.

**(Choice A)** The nucleus accumbens is part of the basal ganglia that mediates reward and pleasure. Transcranial magnetic stimulation targeting this area has been used to treat addiction, but it plays no role in urinary continence.

**(Choice B)** Deep brain stimulation of the subthalamic nucleus has been used to treat the rigidity of Parkinson disease, but it is not involved in urinary continence.

**(Choice C)** The vagus nerve (CN X) is involved in regulating the gastrointestinal system (eg, parasympathetic innervation stimulates gastric muscle contraction and intestinal motility); stimulation is occasionally used to improve gastric motility. However, the vagus nerve does not play a role in micturition or urinary continence.

**(Choice D)** The T6 nerve root contributes to the greater splanchnic nerve (T5-T10), which provides sympathetic innervation to the foregut to slow peristalsis. However, sympathetic stimulation of the bladder, which inhibits detrusor contraction, originates lower, from about T10-L2.

**(Choice E)** The L5 nerve root contributes somatic innervation to many muscles of the lower limb (eg


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**(Choice E)** The L5 nerve root contributes somatic innervation to many muscles of the lower limb (eg, gluteal muscles, tibialis muscles, extensor hallucis longus) but does not innervate the pelvic floor, bladder, or urethral sphincters.

**Educational objective:**
Urge incontinence can be treated with neuromodulation directed toward the S2-S4 nerve roots, which improves pelvic floor muscle strength and contraction of the external urethral sphincter; it may also impact the bladder stretch-contraction reflex.

| Anatomy | Nervous System | Urinary incontinence |
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| Subject | System | Topic |

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A 76-year-old man comes to the office due to severe insomnia of several months' duration. He has trouble falling asleep and feels tired and irritable during the day. The patient's other medical problems include hypertension and a prior cerebrovascular accident with residual right leg weakness. He takes aspirin, rosuvastatin, and lisinopril regularly as prescribed. Temperature is 36.7 C (98.1 F), blood pressure is 118/76 mm Hg, pulse is 62/min, and respirations are 14/min. Examination shows clear lungs with normal S1 and S2. The abdomen is soft and nontender. In addition to nonpharmacologic interventions for insomnia, short-term pharmacologic therapy is being considered. Which of the following medications has the lowest risk of causing adverse effects in this patient?

A. Alprazolam
B. Amitriptyline
C. Clonazepam
D. Diazepam
E. Diphenhydramine
F. Quetiapine



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E. Diphenhydramine
F. Quetiapine
G. Ramelteon



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rosuvastatin, and fish oil regularly as prescribed. Temperature is 36.7°C (98.1°F), blood pressure is 118/76 mm Hg, pulse is 62/min, and respirations are 14/min. Examination shows clear lungs with normal S1 and S2. The abdomen is soft and nontender. In addition to nonpharmacologic interventions for insomnia, short-term pharmacologic therapy is being considered. Which of the following medications has the lowest risk of causing adverse effects in this patient?

- A. Alprazolam (8%)
- B. ~~Amitriptyline~~ (1%)
- C. ~~Clonazepam~~ (2%)
- D. Diazepam (3%)
- E. ~~Diphenhydramine~~ (9%)
- F. Quetiapine (3%)
- G. Ramelteon (71%)

Incorrect
Correct answer

71%

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**Insomnia** is common in the elderly population and can significantly impair quality of life. Nonpharmacologic interventions such as sleep hygiene measures and cognitive-behavioral therapy are recommended for initial management. When nonpharmacologic interventions fail, **pharmacotherapy** may be indicated but must be used with extreme **caution in elderly patients** and should generally be limited to short-term management. Medication selection for elderly patients requires special attention to safety issues due to this population's increased sensitivity to adverse effects of medications in general and sedative-hypnotic agents in particular (eg, oversedation, dizziness, confusion, impaired psychomotor performance, ataxia).

Of the currently available sedative-hypnotic agents, the melatonin agonist **ramelteon** has demonstrated the **lowest side-effect burden** in older adults. Ramelteon binds with high affinity to melatonin receptors in the suprachiasmatic nucleus.

**(Choices A, C, and D)** Benzodiazepines should be avoided in elderly patients due to the increased risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents when taking these medications.

**(Choices B and E)** Amitriptyline, a tricyclic antidepressant, and diphenhydramine, an antihistamine, should be avoided in the elderly due to their strong anticholinergic effects and risks of sedation, delirium, and falls.


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| Side effects of commonly used drugs in the elderly | |
|---|---|
| **Digoxin** | • Arrythmias<br>• Nausea & vomiting<br>• Confusion & weakness |
| **Benzodiazepines** | • Delirium, falls, fractures |
| **1st-generation antihistamines & tricyclic antidepressants** | • Cognitive decline, delirium, hallucination<br>• Orthostatic hypotension, falls<br>• Urinary retention, constipation |
| **Opioid analgesics** | • Constipation<br>• Sedation, confusion, falls |
| **Antipsychotics** | • ↑ Stroke & mortality in dementia patients |
| **Long-acting sulfonylureas** | • Hypoglycemia |
| **Fluoroquinolones** | • Tendon inflammation & rupture |

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**(Choices A, C, and D)** Benzodiazepines should be avoided in elderly patients due to the increased risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents when taking these medications.

**(Choices B and E)** Amitriptyline, a tricyclic antidepressant, and diphenhydramine, an antihistamine, should be avoided in the elderly due to their strong anticholinergic effects and risks of sedation, delirium, and falls.

**(Choice F)** Quetiapine is a second-generation antipsychotic that would not be appropriate as a first-line treatment for insomnia. Antipsychotics carry a risk of increased falls and cardiac mortality in older adults and should not be used without an appropriate indication (eg, psychosis, dangerous agitation).

**Educational objective:**
Benzodiazepines, antihistamines, and sedating antidepressants should be avoided in the treatment of insomnia in elderly patients due to their adverse effects. Ramelteon, a melatonin agonist, has a lower side-effect burden than other sedative-hypnotic agents and is effective in reducing time to sleep onset in the elderly.

**References**

- Review of safety and efficacy of sleep medicines in older adults.
- American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older


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A 34-year-old woman comes to the office due to diplopia, clumsiness of the left hand, and numbness of the right foot. Six months ago, the patient had numbness of the right hand, which resolved without treatment. Ten years ago, she was hurt by an explosion at work that resulted in a metallic foreign body in her left eye. She has no other medical problems and takes no medications. The patient has a 10-pack-year smoking history. Both parents are healthy. Vital signs are normal. BMI is 27 kg/m$^2$. Neurologic examination shows slowing of left eye adduction and left arm power of 4/5 with mild spasticity. Sensation to pinprick is decreased over the right foot. Cerebrospinal fluid analysis shows mononuclear cell pleocytosis and oligoclonal banding. Which of the following pathologic findings is most likely to be present in this patient's brain?

A. Astrocyte shrinkage
B. Eosinophilic inclusions in neurons
C. Extracellular fibrillar protein accumulation
D. Inflammatory vasculitis
E. Local hemorrhage


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A. Astrocyte shrinkage
B. Eosinophilic inclusions in neurons
C. Extracellular fibrillar protein accumulation
D. Inflammatory vasculitis
E. Local hemorrhage
F. Oligodendrocyte depletion



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She has no other medical problems and takes no medications. The patient has a 10-pack-year smoking history. Both parents are healthy. Vital signs are normal. BMI is 27 kg/m$^2$. Neurologic examination shows slowing of left eye adduction and left arm power of 4/5 with mild spasticity. Sensation to pinprick is decreased over the right foot. Cerebrospinal fluid analysis shows mononuclear cell pleocytosis and oligoclonal banding. Which of the following pathologic findings is most likely to be present in this patient's brain?

A. Astrocyte shrinkage (2%)
B. Eosinophilic inclusions in neurons (5%)
C. Extracellular fibrillar protein accumulation (6%)
D. Inflammatory vasculitis (4%)
E. Local hemorrhage (1%)
✓ F. Oligodendrocyte depletion (79%)

Correct
79%
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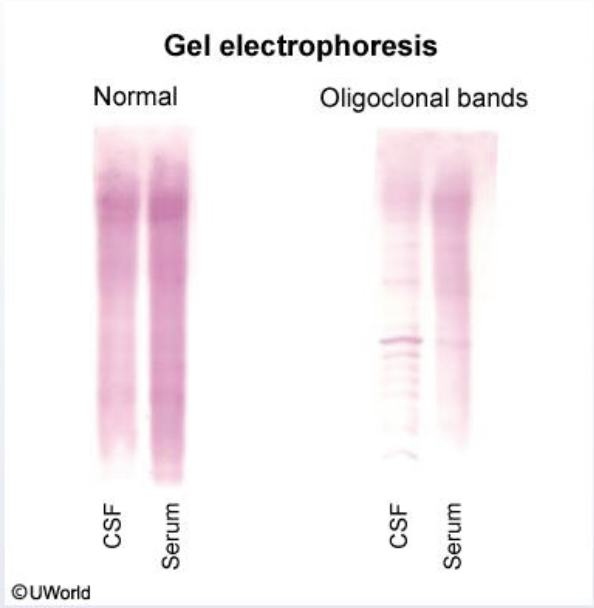


This patient with multiple waxing and waning neurologic deficits that cannot be explained by a single lesion most likely has **multiple sclerosis** (MS). MS is an autoimmune disorder of the **central nervous system** (CNS) characterized by lesions of focal **demyelination**.

Demyelination involves both cellular and humoral immunity. Helper T cells react with myelin antigens and


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Demyelination involves both cellular and humoral immunity. Helper T cells react with myelin antigens and recruit additional lymphocytes and macrophages. Activated $CD8^+$ T cells release cytotoxic granules that injure oligodendrocytes. B cell recruitment leads to the formation of myelin-specific antibodies that activate complement and facilitate myelin breakdown. The result is **oligodendrocyte depletion** with relative sparing of axons.

Diagnosis is largely clinical but is supported by the presence of T2 lesions on MRI (precluded in this patient due to the presence of intraocular metal) or **oligoclonal bands** on cerebrospinal fluid analysis. Oligoclonal bands represent the intrathecal production of immunoglobulins and are highly sensitive for MS. However, oligoclonal bands are nonspecific and may be seen in any CNS disease involving humoral immunity (eg, vasculitis, infection).

**(Choice A)** Astrocytes undergo hypertrophy and hyperplasia, not shrinkage, in response to CNS injury in a process known as glial scarring.

**(Choices B and C)** Both Lewy body dementia and Alzheimer disease are characterized by protein aggregates in brain tissue. Lewy body dementia causes visual hallucinations, dysautonomia, and parkinsonism and is characterized by eosinophilic inclusions in neurons (Lewy bodies). Alzheimer disease causes progressive memory loss and is characterized by extracellular fibrillar protein accumulation



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parkinsonism and is characterized by eosinophilic inclusions in neurons (Lewy bodies). Alzheimer disease causes progressive memory loss and is characterized by extracellular fibrillar protein accumulation (amyloid). Both diseases are uncommon in young patients and are not associated with focal neurologic deficits.

**(Choice D)** Cerebral vasculitis can resemble MS with neurologic deficits that may wax and wane, and oligoclonal bands can be seen. However, patients typically develop severe headache, and systemic symptoms (eg, fever, fatigue, night sweats) are common.

**(Choice E)** Intracerebral hemorrhaging can cause focal deficits, but symptoms would likely have an acute rather than intermittent or relapsing presentation. In addition, lumbar puncture would typically show xanthochromia (yellow-tinged cerebrospinal fluid from blood product breakdown), not a mononuclear pleocytosis.

**Educational objective:**
Multiple sclerosis (MS) is an autoimmune demyelinating disease that results from oligodendrocyte depletion. Within the lesions, inflammatory infiltrates of lymphocytes and macrophages are seen surrounding oligodendrocytes and myelin sheaths. Oligoclonal bands are highly sensitive but nonspecific in patients with MS.


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A previously healthy 16-year-old boy is evaluated for progressive headaches and blurred vision that started several months ago. The headaches are more severe upon waking up in the morning and are often accompanied by nausea and vomiting. He takes no medications and does not use tobacco, alcohol, or illicit drugs. Physical examination is notable for bilateral papilledema. MRI of the brain is shown in the exhibit. This patient's brain lesion most likely originated from which of the following cells?

A. Astrocytes
B. Ependymal cells
C. Microglia
D. Neurons
E. Oligodendrocytes
F. Schwann cells
G. Vascular endothelial cells



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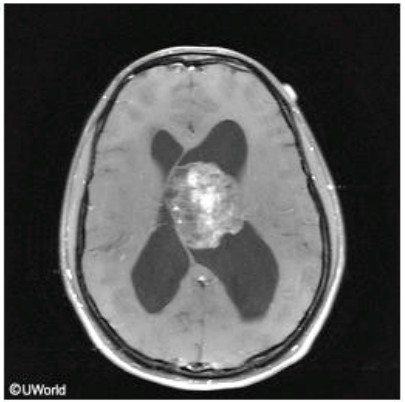


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A previously healthy 16-year-old boy is evaluated for progressive headaches and blurred vision that started several months ago. The headaches are more severe upon waking up in the morning and are often accompanied by nausea and vomiting. He takes no medications and does not use tobacco, alcohol, or illicit drugs. Physical examination is notable for bilateral papilledema. MRI of the brain is shown in the exhibit. This patient's brain lesion most likely originated from which of the following cells?

A. Astrocytes (15%)
B. Ependymal cells (71%)
C. Microglia (3%)
D. Neurons (2%)
E. Oligodendrocytes (3%)
F. Schwann cells (1%)
G. Vascular endothelial cells (2%)



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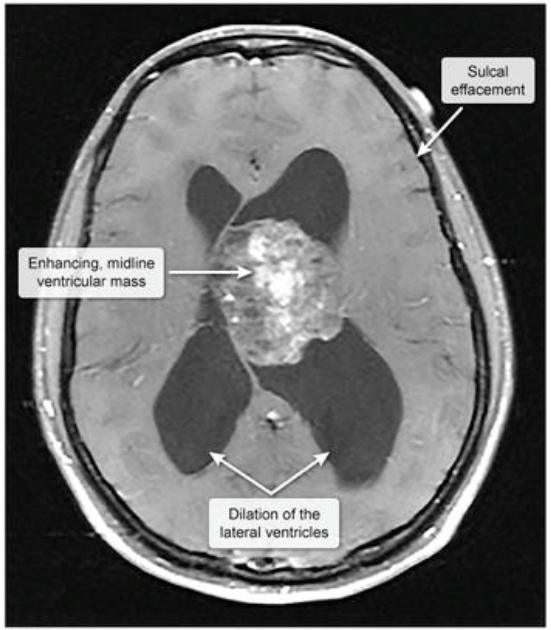
Exhibit Display

Obstructive hydrocephalus

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This patient with **progressive headaches** has an enhancing ventricular mass on MRI, consistent with a ventricular **ependymoma**. Ependymomas arise from **ependymal cells**, which line the walls of the ventricular system and the central canal of the spinal cord and produce cerebrospinal fluid. Choroid plexus tumors (derived from modified ependymal cells) can also be found in the lateral ventricles and have a similar appearance on MRI.

Intraventricular tumors can cause **obstructive (noncommunicating) hydrocephalus** due to impaired flow of cerebrospinal fluid through the interventricular foramina. Hydrocephalus typically manifests with headache, signs of **increased intracranial pressure** (eg, nausea, papilledema, blurred vision), and dilated ventricles on neuroimaging. The diagnosis of ependymoma can be confirmed on histopathologic examination, which shows perivascular pseudorosettes.

**(Choice A)** Astrocytes are the most prevalent type of glial cell in the CNS. Tumors derived from these cells (eg, astrocytoma, glioblastoma) can cause hydrocephalus due to mass effect but are typically found in the brain parenchyma as opposed to the ventricular system.

**(Choice C)** Microglial cells are the phagocytic cells in the CNS. They are not the originators of any major types of CNS tumors.



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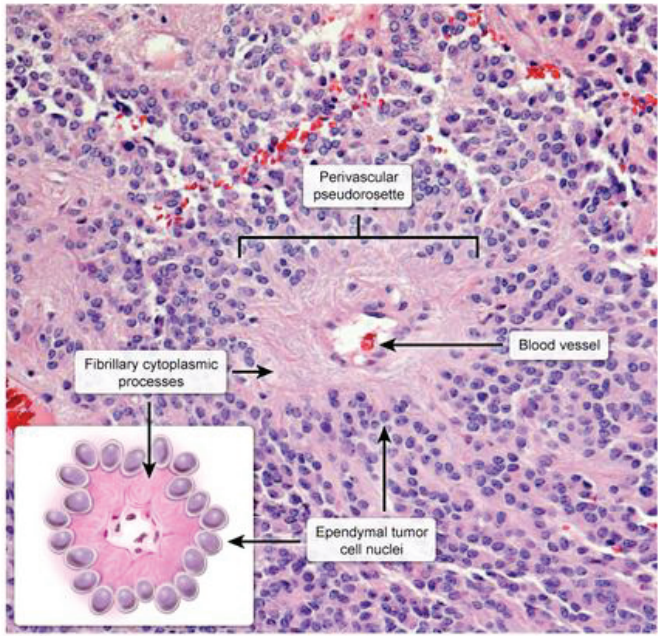
Ependymoma

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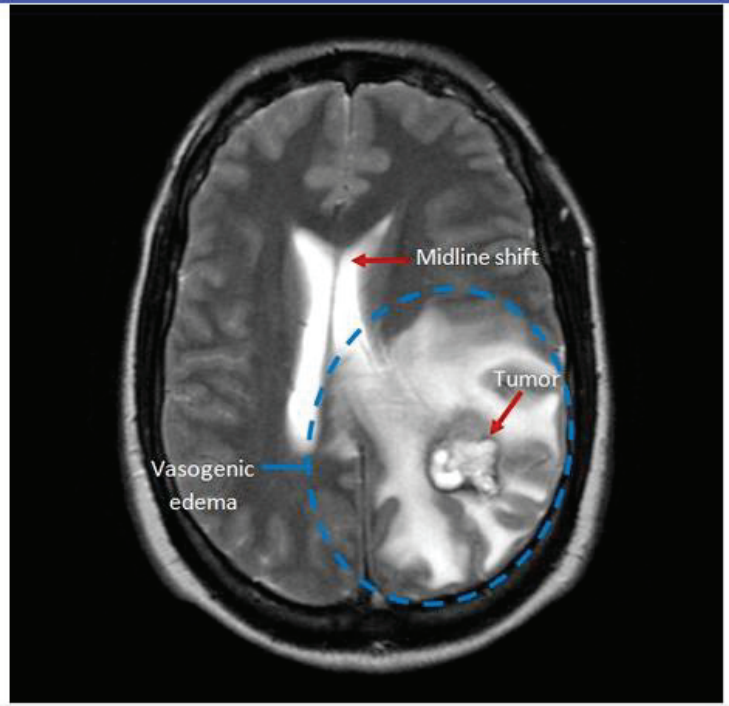


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types of CNS tumors.

**(Choice D)** Brain tumors that arise from neuronal cells are rare, usually found in the brain parenchyma, and more likely to be of mixed neuronal-glial cell origin.

**(Choice E)** Oligodendrocytes are glial cells that are responsible for the myelination of axons in the CNS. Well-differentiated brain tumors arising from oligodendrocytes are referred to as oligodendrogliomas. These tumors, like astrocytomas, occur in the brain parenchyma and not in the ventricular system.

**(Choice F)** Schwann cells form myelin in the peripheral nervous system and serve as the cell of origin for schwannomas, which most commonly occur on upper extremity nerves. Schwannomas that arise from cranial nerves (eg, CN VIII, acoustic neuromas) can cause hydrocephalus from mass effect due to their central location but would not be associated with an intraventricular mass.

**(Choice G)** Hemangioblastomas originate from vascular endothelial cells in the cerebellum or spinal cord. They characteristically appear as an enhancing nodule with a cystic component. These tumors often bleed, which can cause hydrocephalus due to dysfunction in cerebrospinal reabsorption at the arachnoid villi, but they do not originate from the ventricular wall.

**Educational objective:**

Ependymomas originate from the ependymal cells that line the ventricular system and the central canal of


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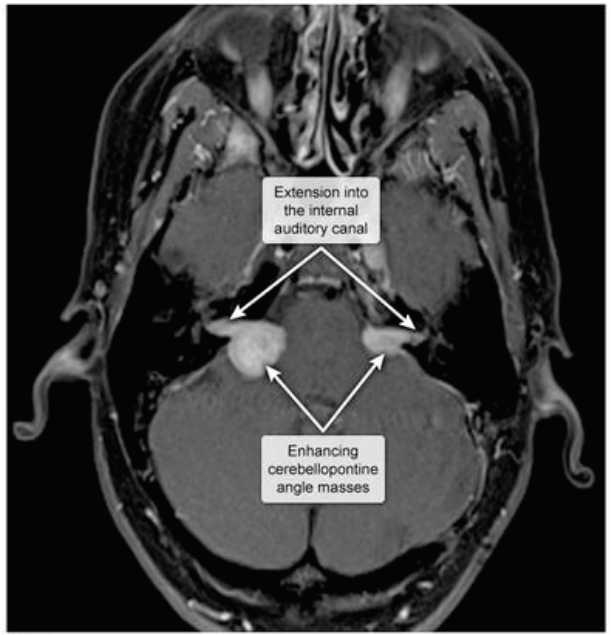
types of CNS tumors.

Exhibit Display

Acoustic neuromas

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Ependymomas originate from the ependymal cells that line the ventricular system and the central canal of



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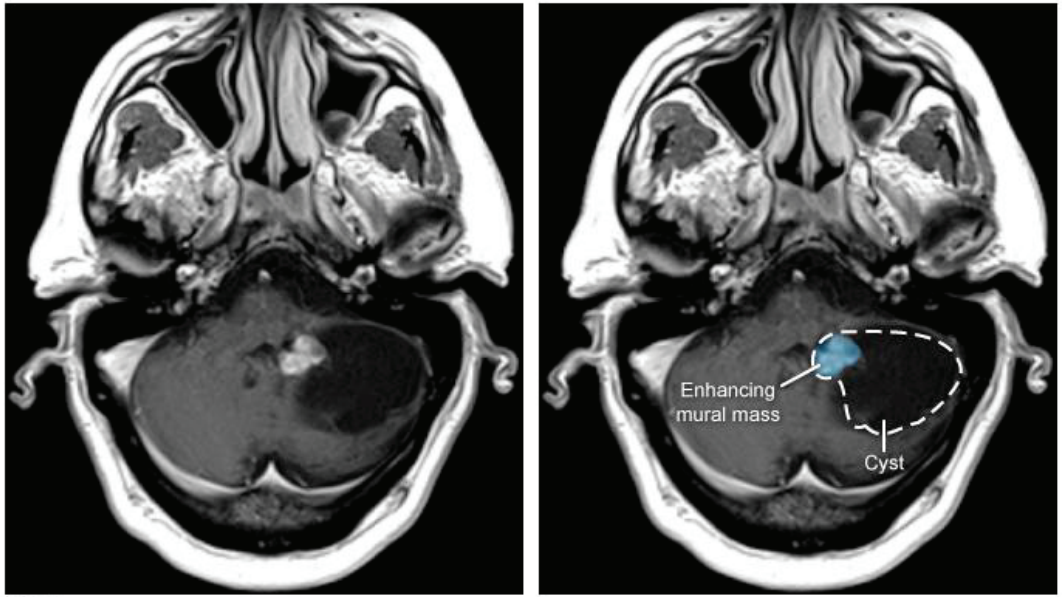
types of CNS tumors.

Exhibit Display

Cerebellar hemangioblastoma

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Ependymomas originate from the ependymal cells that line the ventricular system and the central canal of



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**(Choice F)** Schwann cells form myelin in the peripheral nervous system and serve as the cell of origin for schwannomas, which most commonly occur on upper extremity nerves. Schwannomas that arise from cranial nerves (eg, CN VIII, acoustic neuromas) can cause hydrocephalus from mass effect due to their central location but would not be associated with an intraventricular mass.

**(Choice G)** Hemangioblastomas originate from vascular endothelial cells in the cerebellum or spinal cord. They characteristically appear as an enhancing nodule with a cystic component. These tumors often bleed, which can cause hydrocephalus due to dysfunction in cerebrospinal reabsorption at the arachnoid villi, but they do not originate from the ventricular wall.

**Educational objective:**
Ependymomas originate from the ependymal cells that line the ventricular system and the central canal of the spinal cord. Ventricular ependymomas can block the flow of cerebrospinal fluid through the interventricular foramina, causing signs of increased intracranial pressure (eg, headache, papilledema) due to obstructive (noncommunicating) hydrocephalus.

| Pathology | Nervous System | Brain tumors |
|---|---|---|
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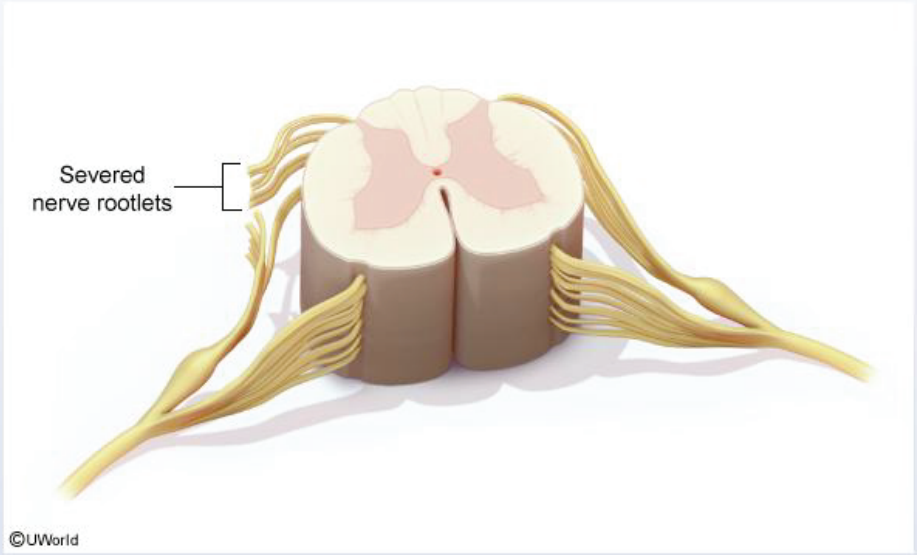
A 6-year-old girl with cerebral palsy undergoes selective dorsal rhizotomy surgery. The patient was born prematurely with a very low birth weight and had experienced periventricular cerebral white matter injury. During the procedure, dorsal rootlets of lumbosacral spinal nerves are selectively severed, as shown in the image below:




Which of the following is the most likely effect of this intervention in this patient's lower extremities?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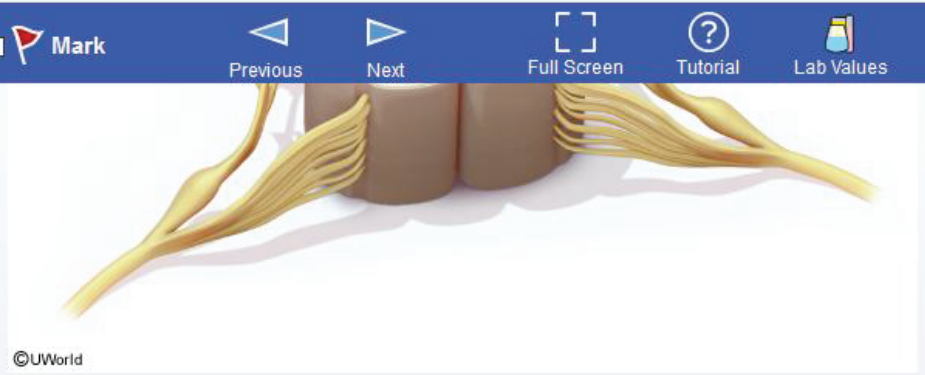


Which of the following is the most likely effect of this intervention in this patient's lower extremities?

A. Decreased muscle mass
B. Decreased muscle tone
C. Increased tendon reflexes
D. Muscle fasciculations
E. Muscle paralysis

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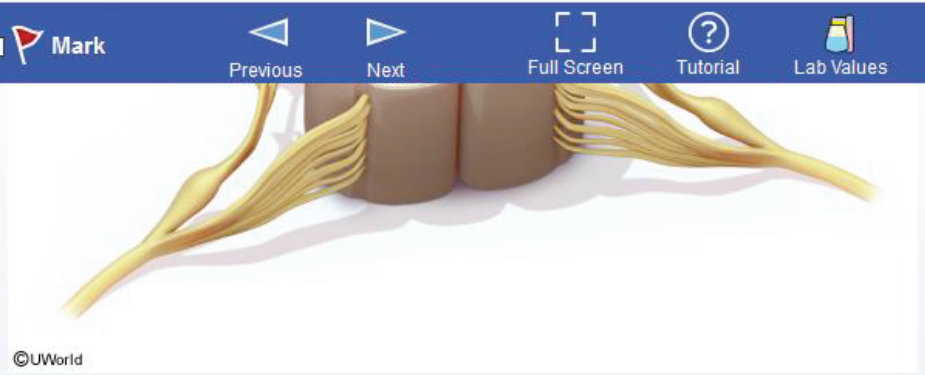


Which of the following is the most likely effect of this intervention in this patient's lower extremities?

A. Decreased muscle mass (5%)
B. Decreased muscle tone (43%)
C. Increased tendon reflexes (24%)
D. Muscle fasciculations (17%)
E. Muscle paralysis (8%)

Correct

43%

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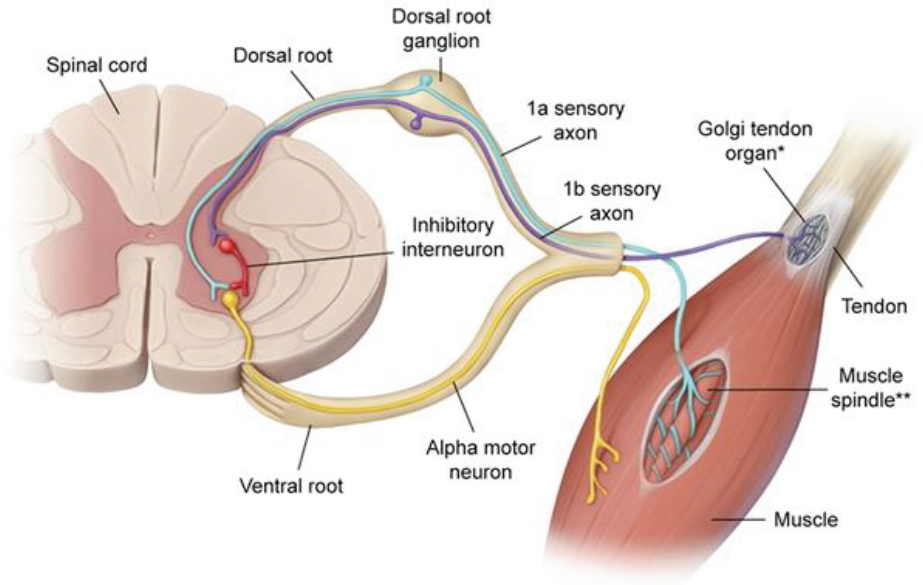
Exhibit Display

## Muscle proprioceptive organs




*Detects changes in muscle tension & inhibits muscle contraction, preventing damage
**Detects changes in muscle length & activates muscle contraction (reflex testing)

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Detects changes in muscle length & activates muscle contraction (reflex testing)
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This patient has cerebral palsy, a heterogeneous condition characterized by permanent, nonprogressive motor dysfunction caused by damage to the developing brain. Certain subtypes result in significant **spasticity** (eg, hypertonia, hyperreflexia). Spastic cerebral palsy may be caused by periventricular white matter necrosis (as in this patient), which leads to a **loss of descending inhibitory control** from the upper motor neurons.

Specifically, lack of CNS inhibition leads to a **hyperactive stretch reflex**. The stretch reflex is a monosynaptic reflex mediated at the level of the spinal cord through the following pathway:

- Muscle lengthening is sensed by muscle spindles
- Afferent signal of stretch is conveyed to the spinal cord via the **dorsal nerve fibers**
- Efferent signals are conveyed via the ventral root of the spinal cord
- Extrafusal fibers are stimulated, causing muscle contraction

The stretch reflex is responsible for deep tendon reflexes (eg, patellar, achilles) and the maintenance of **muscle tone** by constant muscular activity occuring even at rest, so a hyperactive stretch reflex leads to increased muscle tone (ie, spasticity). A selective dorsal rhizotomy procedure **destroys the afferent (sensory) arm** of the reflex arc, decreasing muscle tone without sacrificing motor innervation of the muscles.



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increased muscle tone (ie, spasticity). A selective dorsal rhizotomy procedure **destroys the afferent (sensory) arm** of the reflex arc, decreasing muscle tone without sacrificing motor innervation of the muscles.

**(Choices A, D, and E)** Loss of lower motor neuron innervation can lead to paralysis, muscle atrophy, and fasciculations. However, by damaging only the dorsal nerve rootlets, the motor nerves (ventral) are spared.

**(Choice C)** Deep tendon reflexes are manifestations of the stretch reflex caused by sudden stretching of the muscle. Because this reflex arc is interrupted by dorsal rhizotomy, the procedure results in decreased deep tendon reflexes as well as decreased muscle tone.

**Educational objective:**
Spasticity can be caused by the loss of descending inhibitory signals from upper motor neurons, leading to a hyperactive stretch reflex that results in increased muscle tone. Disruption of the afferent (sensory) arm of the stretch reflex through a selective dorsal rhizotomy can improve spasticity without causing paralysis.

**References**

- Spasticity mechanisms – for the clinician.

Anatomy Nervous System Cerebral palsy


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A 55-year-old man comes to the clinic due to gradual, progressive weakness of the right upper extremity over the past 6 months. Over the last month, he has also noticed weakness in the left upper extremity. Vital signs are normal. Physical examination shows fasciculations and atrophy of the intrinsic muscles of the right hand and the muscles of the forearm. Reflexes are brisk in the upper extremities, and the plantar responses are extensor. Mild gait ataxia is present. Over the course of his illness, this patient will most likely develop which of the following?

A. Decreased left ventricular compliance
B. Decreased lung vital capacity
C. Degeneration of the cardiac conduction system
D. Inability to feel sensations below the neck
E. Refractory generalized tonic-clonic seizures

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A 55-year-old man comes to the clinic due to gradual, progressive weakness of the right upper extremity over the past 6 months. Over the last month, he has also noticed weakness in the left upper extremity. Vital signs are normal. Physical examination shows fasciculations and atrophy of the intrinsic muscles of the right hand and the muscles of the forearm. Reflexes are brisk in the upper extremities, and the plantar responses are extensor. Mild gait ataxia is present. Over the course of his illness, this patient will most likely develop which of the following?

A. Decreased left ventricular compliance (3%)
B. Decreased lung vital capacity (74%)
C. Degeneration of the cardiac conduction system (4%)
D. Inability to feel sensations below the neck (12%)
E. Refractory generalized tonic-clonic seizures (4%)

Correct

74% Answered correctly

01 min, 04 secs Time Spent

11/11/2020 Last Updated



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This patient has progressive weakness with signs of **upper motor neuron** (UMN) dysfunction (eg, brisk reflexes, extensor plantar reflex) and **lower motor neuron** (LMN) dysfunction (eg, fasciculations, muscle atrophy), which is characteristic of **amyotrophic lateral sclerosis** (ALS), a terminal neurodegenerative disease.

Patients with ALS most often die of **respiratory failure**, which is caused by multiple factors:

- Inspiratory muscle (eg, diaphragm) atrophy and weakness, which leads to poor inspiratory strength. This is evident on pulmonary function testing as **decreased vital capacity** (the maximum volume displaced from the lung), which is followed as a **marker of disease progression** in patients with ALS.
- Expiratory muscle weakness, which leads to an **ineffective cough** and poor airway clearance.
- Bulbar muscle weakness, which leads to dysphagia and **chronic aspiration**.

Treatment of ALS often focuses on improving respiratory function, which both prolongs survival and improves quality of life.

**(Choice A)** Friedreich ataxia also presents with gait abnormalities and limb weakness. Death is typically due to cardiac dysfunction, due to either abnormalities of the cardiac conduction system or cardiac muscle defects (eg, decreased left ventricular compliance). However, Friedreich ataxia occurs in children age 5-15


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years.

**(Choice C)** Disseminated Lyme disease can present with radiculopathy; the classic triad of neurologic Lyme is meningitis, cranial neuropathy, and radiculoneuropathy (sensory or motor). Carditis can also occur, which can result in degeneration of the cardiac conduction system. However, this patient's combination of UMN and LMN signs is much more likely to be ALS.

**(Choice D)** ALS is a disease that primarily affects motor neurons (both upper and lower). Although sensory disturbances can be present in some patients, widespread sensory defects do not occur.

**(Choice E)** Tuberous sclerosis is an autosomal dominant disorder that results in tumors in multiple organ systems. Generalized tonic-clonic seizures often occur and become refractory as the disease progresses. This patient has no evidence of tumors or seizures nor a positive family history to suggest tuberous sclerosis.

**Educational objective:**
Patients with amyotrophic lateral sclerosis often develop respiratory failure due to inspiratory muscle weakness (causing decreased vital capacity), expiratory muscle weakness (causing a weak cough), and bulbar dysfunction (causing dysphagia and chronic aspiration).



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An 11-month-old boy is brought to the office due to irregular jerking movements. His mother states that for 2 weeks he has looked pale and tired, and he has been more fussy and less playful than usual. Temperature is 36.7 C (98 F), blood pressure is 100/60 mm Hg, pulse is 114/min, and respirations are 16/min. Physical examination reveals spontaneous bursts of nonrhythmic conjugate eye movements in various directions. The patient also has myoclonus involving the trunk and limbs as well as generalized hypotonia. A right-sided, nontender, immobile abdominal mass is palpated. There is no hepatosplenomegaly, and bowel sounds are normal. Complete blood count reveals anemia, and urine is positive for elevated levels of catecholamine breakdown products. Which of the following is the most likely diagnosis?

A. Carcinoid tumor
B. Ewing sarcoma
C. Medulloblastoma
D. Neuroblastoma
E. Non-Hodgkin lymphoma



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To/min. Physical examination reveals spontaneous bursts of nonrhythmic conjugate eye movements in various directions. The patient also has myoclonus involving the trunk and limbs as well as generalized hypotonia. A right-sided, nontender, immobile abdominal mass is palpated. There is no hepatosplenomegaly, and bowel sounds are normal. Complete blood count reveals anemia, and urine is positive for elevated levels of catecholamine breakdown products. Which of the following is the most likely diagnosis?

A. Carcinoid tumor
B. Ewing sarcoma
C. Medulloblastoma
D. Neuroblastoma
E. Non-Hodgkin lymphoma
F. Pheochromocytoma
G. Wilms tumor

Submit



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To/min. Physical examination reveals spontaneous bursts of nonrhythmic conjugate eye movements in various directions. The patient also has myoclonus involving the trunk and limbs as well as generalized hypotonia. A right-sided, nontender, immobile abdominal mass is palpated. There is no hepatosplenomegaly, and bowel sounds are normal. Complete blood count reveals anemia, and urine is positive for elevated levels of catecholamine breakdown products. Which of the following is the most likely diagnosis?

A. ~~Carcinoid tumor~~ (4%)
B. ~~Ewing sarcoma~~ (0%)
C. ~~Medulloblastoma~~ (5%)
D. Neuroblastoma (49%)
E. ~~Non-Hodgkin lymphoma~~ (0%)
F. ~~Pheochromocytoma~~ (25%)
G. Wilms tumor (14%)



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Explanation

| Neuroblastoma | |
|---|---|
| **Pathogenesis** | • Neural crest origin<br>• Involves adrenal medulla, sympathetic chain |
| **Clinical features** | • Median age <2<br>• Abdominal mass<br>• Periorbital ecchymoses (orbital metastases)<br>• Spinal cord compression from epidural invasion ("dumbbell tumor")<br>• Opsoclonus-myoclonus syndrome |
| **Diagnostic findings** | • Elevated catecholamine metabolites<br>• Small, round blue cells on histology<br>• *N-myc* gene amplification |

Nonrhythmic conjugate eye movements and involuntary jerking movements of the trunk and limbs (**opsoclonus-myoclonus syndrome**) in a young patient should prompt evaluation for **neuroblastoma**.

This is the most common extracranial solid neoplasm of childhood and arises from neural crest cells of the



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Nonrhythmic conjugate eye movements and involuntary jerking movements of the trunk and limbs (**opsoclonus-myoclonus syndrome**) in a young patient should prompt evaluation for **neuroblastoma**. This is the most common extracranial solid neoplasm of childhood and arises from neural crest cells of the adrenal medulla or sympathetic ganglia.

Patients typically present at age <2 with a firm **abdominal mass**, most often involving the adrenal gland, and constitutional symptoms (eg, weight loss, fatigue). Bone marrow infiltration can cause anemia or pancytopenia, and orbital metastases may result in proptosis and/or **periorbital ecchymoses**. Although rare, opsoclonus-myoclonus is a paraneoplastic syndrome highly associated with neuroblastoma and is believed to be an autoantibody response to central nervous system antigens.

The majority of patients with neuroblastoma have **elevated catecholamine metabolites** (eg, HVA, VMA) due to the neural crest origin. Biopsy of the mass is diagnostic and will reveal small round blue cells and Homer Wright rosettes. Tumor tissue is subsequently tested for ***N-myc* amplification**, which predicts a poor prognosis.

**(Choice A)** Carcinoid tumor is a neuroendocrine tumor that is rare in children. Tumor secretion of serotonin causes carcinoid syndrome (eg, flushing, diarrhea, bronchospasm) and increased 5-hydroxyindoleacetic acid (serotonin metabolite) in the urine.



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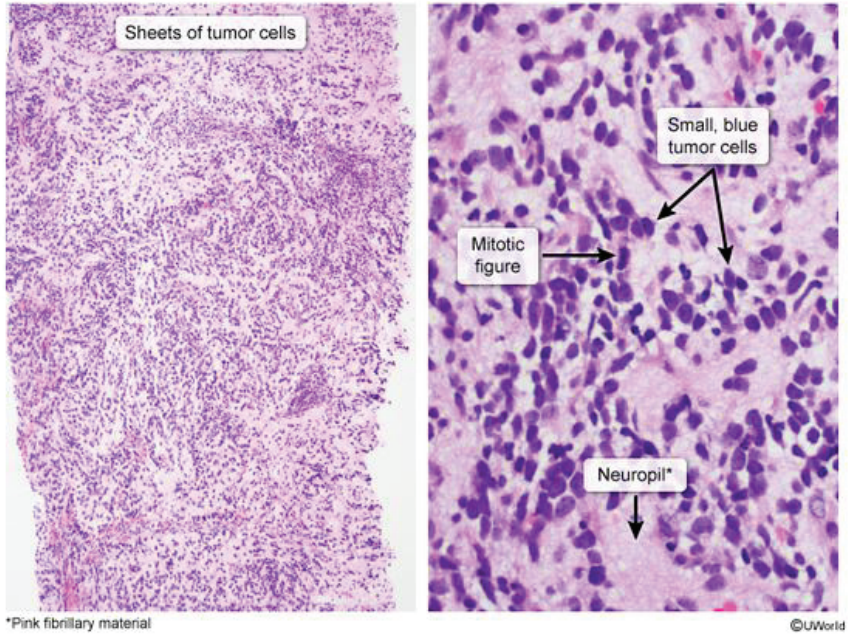
Exhibit Display

**Neuroblastoma**

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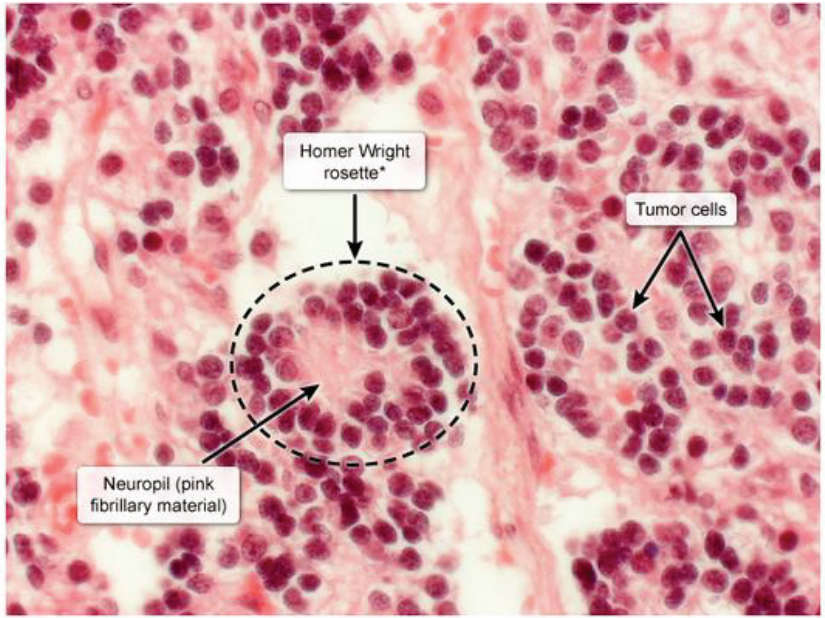
Neuroblastoma




*Tumor cells arranged around central neuropil core

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5-hydroxyindoleacetic acid (serotonin metabolite) in the urine.

**(Choice B)** Ewing sarcoma is a malignant bone tumor that arises predominantly in long bones. This neoplasm typically presents in older children and teenagers with pain and swelling over the mass.

**(Choice C)** Medulloblastoma is the most common malignant brain tumor in children. It arises in the cerebellum and causes ataxia, not opsoclonus-myoclonus. As in neuroblastoma, Homer Wright rosettes may be identified; however, urine catecholamine metabolites would not be present.

**(Choice E)** Non-Hodgkin lymphoma can present as an abdominal mass but is rare in infants and not associated with opsoclonus-myoclonus or increased urine catecholamines.

**(Choice F)** Pheochromocytoma is an adrenal tumor that also secretes catecholamines; however, this neoplasm occurs more commonly in adults and is not associated with opsoclonus-myoclonus.

**(Choice G)** Wilms tumor is a renal cancer that presents in early childhood (median age 3-4) with an abdominal/flank mass. In contrast to neuroblastoma, Wilms tumor does not cause opsoclonus-myoclonus or result in catecholamines in the urine.

**Educational objective:**

Opsoclonus-myoclonus is a paraneoplastic syndrome associated with neuroblastoma, the most common extracranial solid neoplasm in children. The tumor typically arises from the neural crest cells of the adrenal


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cerebellum and causes ataxia, not opsoclonus-myoclonus. As in neuroblastoma, Homer Wright rosettes may be identified; however, urine catecholamine metabolites would not be present.

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**Educational objective:**

Opsoclonus-myoclonus is a paraneoplastic syndrome associated with neuroblastoma, the most common extracranial solid neoplasm in children. The tumor typically arises from the neural crest cells of the adrenal medulla and presents with an abdominal mass and elevated catecholamine breakdown products.

**References**

- Neuroblastoma presenting as opsoclonus-myoclonus: a series of six cases and review of literature.



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A 64-year-old man is hospitalized with abdominal pain, nausea, and vomiting. The patient has had several similar episodes in the past and was advised to avoid alcohol consumption. Evaluation reveals epigastric tenderness and elevated serum amylase and lipase levels. The patient is admitted, and treatment with bowel rest and intravenous fluids is begun. During hospitalization, he develops new-onset confusion. Physical examination shows horizontal nystagmus and gait ataxia. Brain imaging reveals abnormalities in the mammillary bodies and periaqueductal gray matter. Which of the following most likely precipitated this patient's current neurologic condition?

A. Abrupt alcohol cessation
B. Excessive hydration
C. Glucose infusion
D. Hypotonic fluid administration
E. Lack of anticoagulant use
F. Vitamin supplementation



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A. Abrupt alcohol cessation (15%)
B. Excessive hydration (5%)
C. Glucose infusion (64%)
D. Hypotonic fluid administration (8%)
E. Lack of anticoagulant use (0%)
F. Vitamin supplementation (5%)

Correct

64%
Answered correctly

31 secs
Time Spent

10/18/2020
Last Updated



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| Features of Wernicke-Korsakoff syndrome | |
|---|---|
| **Associated conditions** | • Chronic **alcoholism** (most common)<br>• Malnutrition |
| **Pathophysiology** | • **Thiamine deficiency** → impairs ATP generation → neuronal dysfunction/death<br>• Paraventricular lesions (eg, **mammillary bodies**, dorsomedial thalamus) |
| **Clinical findings** | • **Confusion**<br>• **Oculomotor dysfunction** (eg, horizontal nystagmus & bilateral abducens palsy)<br>• Postural & gait **ataxia**<br>• Memory impairment (permanent) |
| **Treatment** | • Intravenous thiamine<br>• Administration of glucose before thiamine can worsen symptoms |

This patient with pancreatitis (nausea/vomiting, abdominal pain, elevated lipase) and a history of alcohol


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| | |
|---|---|
| | • Administration of glucose before thiamine can worsen symptoms |

This patient with pancreatitis (nausea/vomiting, abdominal pain, elevated lipase) and a history of alcohol abuse received intravenous fluids and developed the classic triad of **Wernicke encephalopathy** (WE):

- **Oculomotor dysfunction**: horizontal nystagmus, lateral rectus palsy, ophthalmoplegia
- **Gait ataxia**: slow, wide-based gait; postural ataxia
- **Encephalopathy**: confusion, apathy, inattentiveness, disorientation

WE is a complication of **thiamine (vitamin $B_1$) deficiency** and most commonly occurs in patients with a history of long-standing **alcohol abuse** or other forms of chronic malnourishment (eg, anorexia, short-bowel syndrome). Thiamine is a vitamin cofactor for multiple enzymes involved in glucose metabolism, and deficiency results in the brain's inability to utilize glucose, leading to neuronal damage and necrosis. Iatrogenic WE can be precipitated by the administration of **glucose-containing fluids** (this patient likely received these as a maintenance fluid), which deplete the last remaining stores of thiamine. Areas of the brain with high metabolic demand are particularly susceptible; focal hemorrhage or atrophy of the **mammillary bodies** is characteristic. The periaqueductal gray, thalamus, and medulla may also be affected.


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Intravenous thiamine should be administered before infusion of glucose-containing fluids in at-risk patients and in all patients with suspected WE. Ocular irregularities are the first to respond to thiamine and typically normalize within hours. Gait ataxia and confusion typically respond over the course of days to weeks.

**(Choice A)** Abrupt alcohol cessation can cause alcohol withdrawal. Tremor and diaphoresis are common and may progress to delirium, seizures, and death. Ataxia and ophthalmoplegia are unexpected.

**(Choice B)** Chronic hyponatremia can occur in patients with heavy alcohol use. Overly rapid correction with normal saline causes osmotic demyelination syndrome, which manifests as dysarthria, confusion, and paralysis. Some patients become "locked in" (ie, alert but unable to move or verbally communicate); however, extraocular muscles are spared.

**(Choice D)** Hypotonic fluid administration can result in acute hyponatremia, which can cause cerebral edema. Symptoms are typically progressive, with headache and nausea occurring before alterations in mental status. Ophthalmoplegia and ataxia are unexpected.

**(Choice E)** Prophylactic low-dose anticoagulation is typically recommended to prevent deep venous thrombosis (DVT) in patients with prolonged hospitalization or inactivity. Pulmonary embolism, the most common sequela of DVT, typically causes pleuritic chest pain, tachycardia, and dyspnea.


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edema. Symptoms are typically progressive, with headache and nausea occurring before alterations in mental status. Ophthalmoplegia and ataxia are unexpected.

**(Choice E)** Prophylactic low-dose anticoagulation is typically recommended to prevent deep venous thrombosis (DVT) in patients with prolonged hospitalization or inactivity. Pulmonary embolism, the most common sequela of DVT, typically causes pleuritic chest pain, tachycardia, and dyspnea.

**(Choice F)** Thiamine supplementation is used for both prevention and treatment of WE; it does not precipitate the disease.

**Educational objective:**
Wernicke encephalopathy is a complication of thiamine deficiency characterized by encephalopathy, ataxia, and oculomotor dysfunction. It occurs most commonly in patients with chronic alcohol abuse and may be precipitated by infusion of glucose-containing fluids. Neuroimaging reveals focal hemorrhage or atrophy of the mammillary bodies.

| Pathology | Nervous System | Wernicke korsakoff syndrome |
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| Subject | System | Topic |

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A 5-year-old Caucasian boy is brought to the physician's office with recent-onset gait instability and gait ataxia. MRI of the brain shows a midline posterior fossa mass. Biopsy of the mass reveals sheets of primitive cells and many mitotic figures. This patient most likely suffers from which of the following?

A. Pilocytic astrocytoma
B. Glioblastoma
C. Oligodendroglioma
D. Ependymoma
E. Medulloblastoma
F. Primary CNS lymphoma
G. Meningioma
H. Craniopharyngioma
I. Schwannoma
J. Pituitary adenoma



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C. Oligodendroglioma
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I. Schwannoma
J. Pituitary adenoma



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primitive cells and many mitotic figures. This patient most likely suffers from which of the following?

A. Pilocytic astrocytoma (20%)
B. ~~Glioblastoma~~ (4%)
C. ~~Oligodendroglioma~~ (1%)
D. ~~Ependymoma~~ (4%)
✓ E. Medulloblastoma (60%)
F. ~~Primary CNS lymphoma~~ (0%)
G. ~~Meningioma~~ (1%)
H. ~~Craniopharyngioma~~ (5%)
I. ~~Schwannoma~~ (0%)
J. ~~Pituitary adenoma~~ (0%)

Correct

60%

01 min, 21 secs

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Gait instability and limb ataxia are symptoms of cerebellar involvement. The mass described indicates that a brain tumor is causing the cerebellar symptoms in this child. Because both pilocytic astrocytomas and medulloblastomas arise in the cerebellum, microscopic findings must be relied on to determine which type of tumor this patient has. Sheets of primitive cells with many mitotic figures described in the vignette indicate a medulloblastoma, not a pilocytic astrocytoma. Medulloblastomas are part of a group called "primitive neuroectodermal tumors" (PNETs). PNETs are composed of sheets of small cells with deeply basophilic nuclei and scant cytoplasm (small, round, blue cells). Abundant mitoses are also seen. Medulloblastomas are undifferentiated and aggressive tumors.

The cerebellar vermis is the most common location of a medulloblastoma. Symptoms include signs of **increased intracranial pressure** (morning headaches, vomiting, and lethargy). **Cerebellar dysfunction** occurs as the tumor compresses adjacent structures.

**(Choice A)** Pilocytic astrocytoma is the most common brain neoplasm of childhood. Although both pilocytic astrocytomas and medulloblastomas are often located in the cerebellum, they can be differentiated by histology. On microscopic examination of a pilocytic astrocytoma, pilocytic astrocytes and Rosenthal fibers are seen. Pilocytic astrocytomas are low-grade tumors and have a better prognosis than medulloblastomas.



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**(Choice A)** Pilocytic astrocytoma is the most common brain neoplasm of childhood. Although both pilocytic astrocytomas and medulloblastomas are often located in the cerebellum, they can be differentiated by histology. On microscopic examination of a pilocytic astrocytoma, pilocytic astrocytes and Rosenthal fibers are seen. Pilocytic astrocytomas are low-grade tumors and have a better prognosis than medulloblastomas.

**(Choice D)** Ependymomas are the third most common brain neoplasm found in children. They arise in the walls of the ventriculi and can hamper CSF flow and cause hydrocephalus. On microscopic examination, ependymal cells form gland-like structures called "rosettes."

**Educational Objective:**

Medulloblastoma is the second most common brain neoplasm of childhood. It is located in the cerebellum, often at the vermis, and consists of sheets of small, blue cells. Like other "PNET" tumors, medulloblastomas are poorly differentiated and have a bad prognosis.

| Pathology | Nervous System | Brain tumors |
|---|---|---|
| Subject | System | Topic |

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A 26-year-old woman is brought to the emergency department due to acute-onset diplopia. Medical history is significant for episodes of blurry vision involving her right eye that occurred 6 months and 2 years ago. These episodes were associated with deficits in color vision and pain made worse with eye movement. The patient recovered the majority of her visual acuity after a few months in both cases. On neurologic examination, she has a visual acuity of 20/20 OS and 20/40 OD, mild right optic disk atrophy, and a relative afferent pupillary defect in the right eye. There is slowed and impaired adduction of the left eye with right lateral gaze. Convergence testing shows normal adduction in both eyes. The remainder of the neurologic examination is unremarkable. This patient's diplopia is most likely caused by which of the following mechanisms?

A. Impaired neuromuscular transmission
B. Loss of axons
C. Muscle fiber inflammation and necrosis
D. Nerve compression
E. Reduced saltatory conduction



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A. Impaired neuromuscular transmission (8%)
B. Loss of axons (10%)
C. Muscle fiber inflammation and necrosis (4%)
D. Nerve compression (8%)
✓ E. Reduced saltatory conduction (67%)

67% 02 mins, 09 secs 02/24/2021


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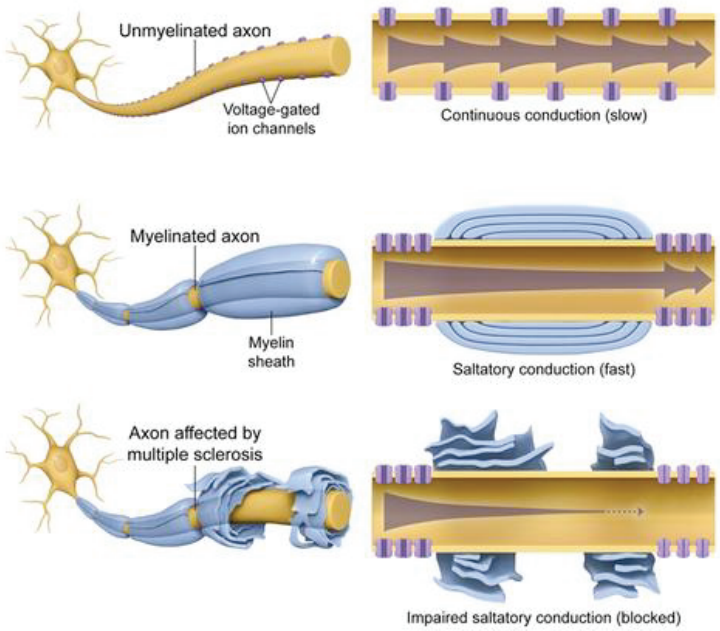
Action potential propagation

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Impaired saltatory conduction (blocked)

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This young woman has diplopia with features of internuclear ophthalmoplegia (impaired adduction on the left with right lateral gaze). This, along with her prior episodes of optic neuritis (transient blurred vision and eye pain with movement), raises concern for **multiple sclerosis (MS)**, a demyelinating disease of the central nervous system (CNS) caused by an autoimmune response directed at oligodendrocytes.

In unmyelinated neurons, signal transmission requires sequential activation of adjacent sodium channels down the entire length of the axon. In myelinated neurons, the depolarization impulse is regenerated at discrete points along the axon (nodes of Ranvier) where sodium channels are concentrated. The myelin sheath serves as an electrical insulator that results in the impulse "jumping" between 2 adjacent nodes **(saltatory conduction)**. This process allows for myelinated neurons to transmit impulses >10x faster than unmyelinated neurons.

Due to the **acute demyelination** seen with MS, propagation of the impulse cannot occur, as the distance between the sodium channels at the nodes of Ranvier precludes sequential activation. This causes a **conduction block**. Over time, sodium channels eventually redistribute across the naked axon and surviving oligodendrocytes partially remyelinate neurons, allowing for some restoration of signal transmission (explaining why some of the symptoms and signs of MS resolve to a variable extent).



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Impaired saltatory conduction (blocked)

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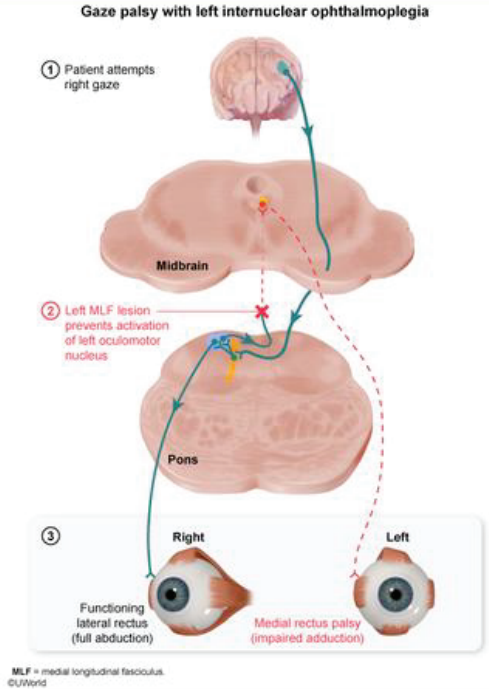


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transmission (explaining why some of the symptoms and signs of MS resolve to a variable extent).



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transmission (explaining why some of the symptoms and signs of MS resolve to a variable extent).

**(Choice A)** Impaired neuromuscular transmission can be seen in myasthenia gravis, which is caused by autoantibodies against acetylcholine receptors at the neuromuscular junction. Affected patients typically present with fluctuating diplopia, ptosis, and/or bulbar muscle weakness.

**(Choice B)** Loss of axons and neurons occurs over time in *chronic* multiple sclerosis plaques. This patient had prior episodes of optic neuritis that have resolved. However, the internuclear ophthalmoplegia is acute and would demonstrate a relative preservation of axons.

**(Choice C)** Muscle fiber inflammation and necrosis can be seen with various forms of myositis (eg, polymyositis, dermatomyositis, inclusion body myositis). Muscle disorders rarely follow a relapsing-remitting course and are not associated with optic neuritis or internuclear ophthalmoplegia.

**(Choice D)** Optic nerve compression would most likely result in progressive vision loss. This patient's symptoms are more consistent with a relapsing-remitting disease pattern with lesions affecting multiple nervous system locations.

**Educational objective:**
Multiple sclerosis is an autoimmune disorder of the central nervous system characterized by recurrent episodes of demyelination, leading to reduced saltatory conduction. Internuclear ophthalmoplegia and


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autoantibodies against acetylcholine receptors at the neuromuscular junction. Affected patients typically present with fluctuating diplopia, ptosis, and/or bulbar muscle weakness.

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**(Choice D)** Optic nerve compression would most likely result in progressive vision loss. This patient's symptoms are more consistent with a relapsing-remitting disease pattern with lesions affecting multiple nervous system locations.

**Educational objective:**
Multiple sclerosis is an autoimmune disorder of the central nervous system characterized by recurrent episodes of demyelination, leading to reduced saltatory conduction. Internuclear ophthalmoplegia and optic neuritis are common manifestations.



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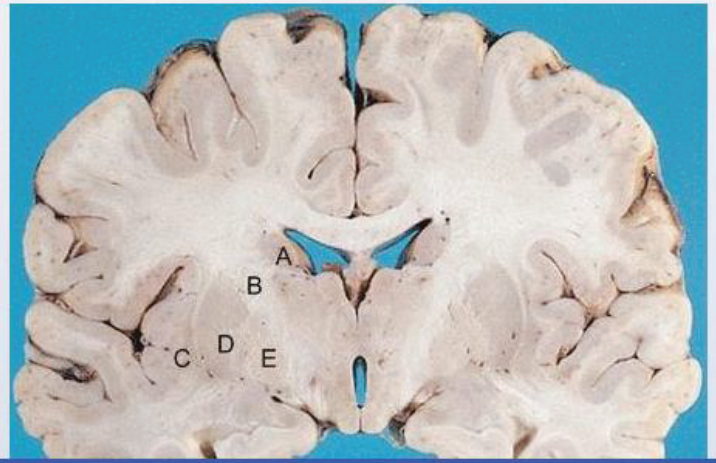
A 38-year-old man is brought to the office for evaluation of behavioral changes. His wife says the patient has had frequent outbursts of anger, depressive mood, and insomnia. The patient recently lost his job as a machine operator because of lack of focus and poor memory. Over the past several years, he also has had involuntary, jerky, nonpurposeful movements of the extremities and face that have progressively worsened. These abnormal movements are present while he is awake but not during sleep. His 55-year-old mother has similar abnormal body movements and is at a nursing home with dementia. Which of the following labeled regions of a normal brain is most likely to be affected by this patient's disease process?





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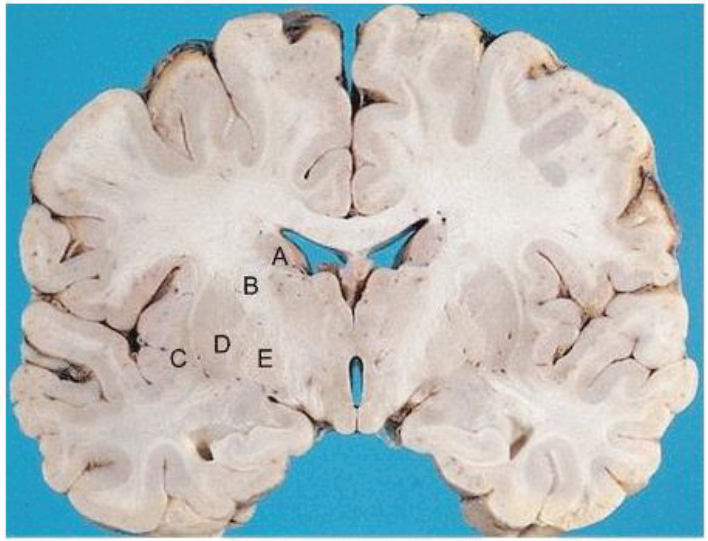


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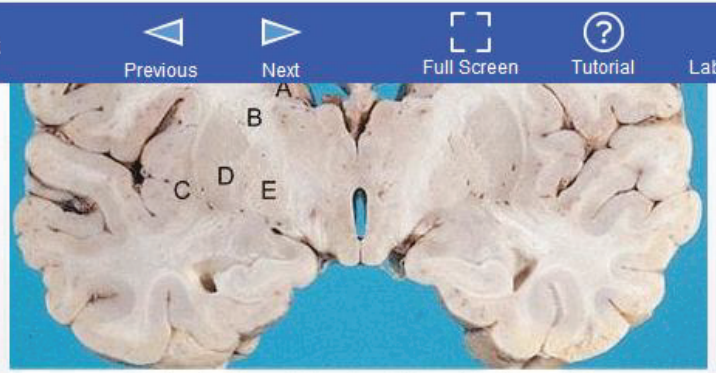


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- A.A
- B.B
- C.C
- D.D
- E.E

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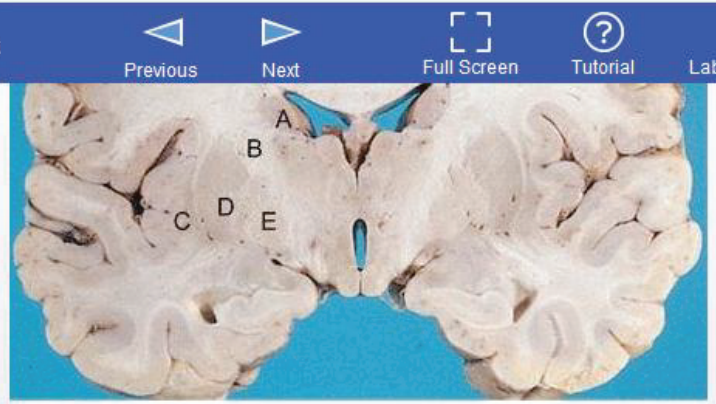


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- A.A (69%)
- B.B (2%)
- C.C (3%)
- D.D (13%)
- E.E (10%)



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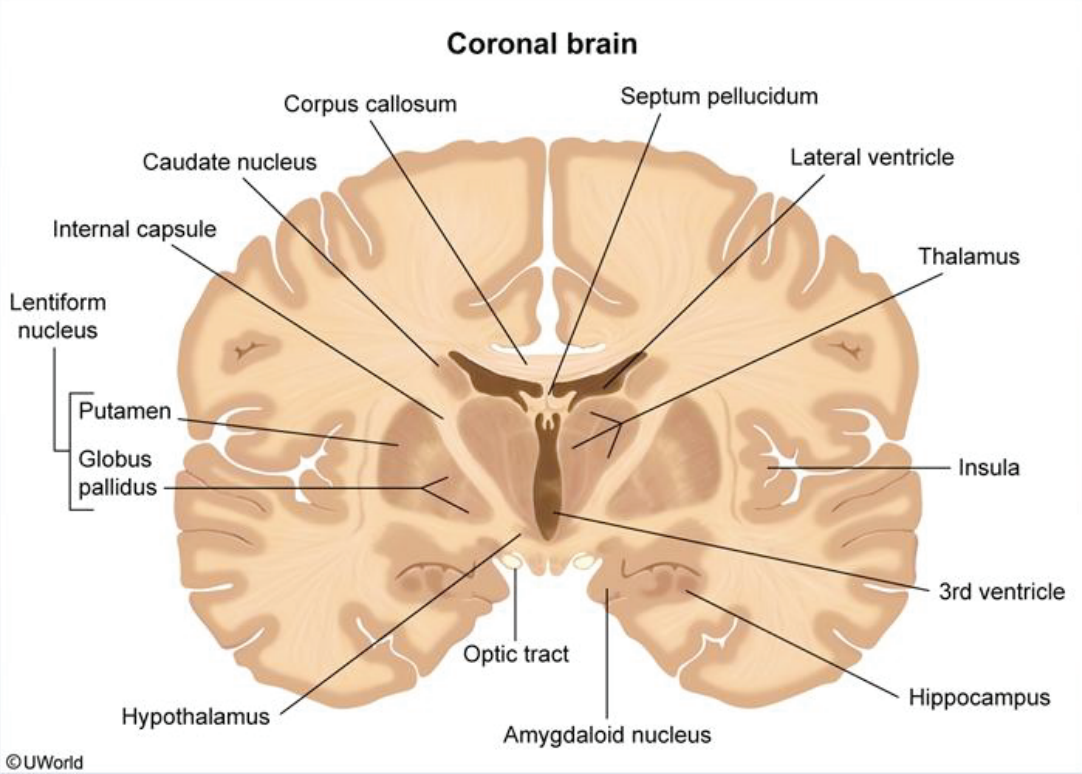




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This patient's cognitive decline, chorea (jerky, nonpurposeful movements), and family history of similar symptoms are highly suggestive of **Huntington disease** (HD). This autosomal dominant disease results from an excessive number of **CAG trinucleotide repeats** in the huntingtin gene, causing a gain-of-function mutation that results in the accumulation of toxic mutant huntingtin protein. The abnormal protein buildup causes **loss of inhibitory (GABA) neurons** in the caudate nucleus, leading to the characteristic movement abnormalities observed in HD.

Although the diagnosis of HD is confirmed by genetic analysis, imaging studies can support the clinical findings and typically show **atrophy of the caudate nuclei**, causing enlargement of the lateral ventricles. The caudate nucleus is a curved or C-shaped structure in its complete form. The head of the caudate can be identified in the inferolateral walls of the frontal horns of the lateral ventricles. The caudate nucleus and putamen together make up the striatum, which is critical for movement control and coordination along with behavioral regulation.

**(Choice B)** This structure is the internal capsule. The anterior limb of the internal capsule separates the caudate nucleus from the globus pallidus and putamen and carries a portion of the thalamocortical fibers. The posterior limb of the internal capsule separates the globus pallidus and putamen from the thalamus and carries corticospinal motor and somatic sensory fibers as well as visual and auditory fibers.



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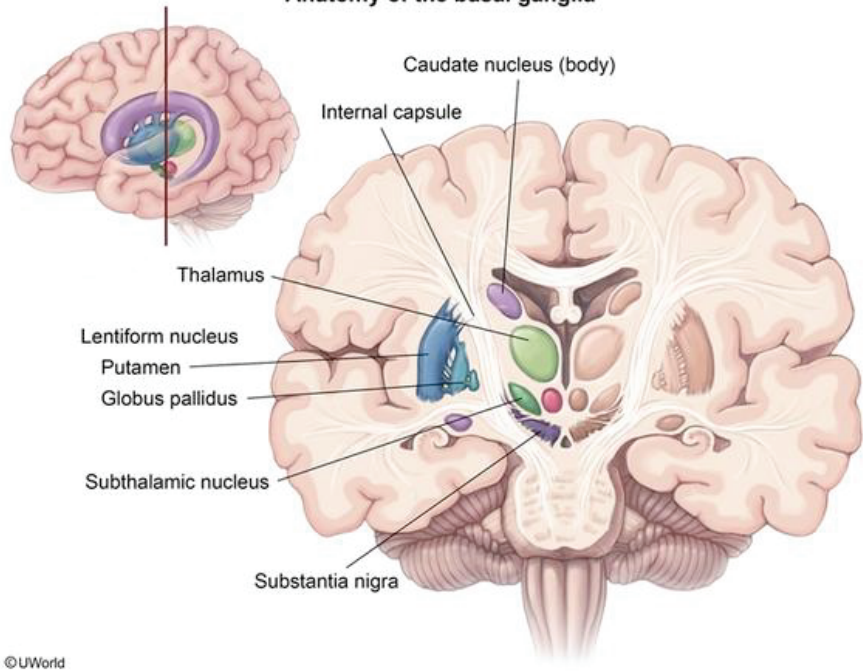
Anatomy of the basal ganglia

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caudate nucleus from the globus pallidus and putamen and carries a portion of the thalamocortical fibers. The posterior limb of the internal capsule separates the globus pallidus and putamen from the thalamus and carries corticospinal motor and somatic sensory fibers as well as visual and auditory fibers.

**(Choice C)** This structure is the insular cortex (insula). The insula plays a role in the limbic system (emotion) as well as in the coordination of some autonomic functions.

**(Choice D)** Although the putamen does atrophy in Huntington disease, this change is not as significant or as specific to Huntington disease as atrophy of the caudate nucleus.

**(Choice E)** Atrophy of the globus pallidus is observed late in the progression of HD when generalized cortical atrophy occurs.

**Educational objective:**
The head of the caudate lies in the inferolateral wall of the frontal horn of the lateral ventricle. It is separated from the globus pallidus and putamen by the internal capsule. Atrophy of the caudate nuclei with enlargement of the lateral ventricles is characteristic of Huntington disease and can be observed on neuroimaging.

Anatomy Nervous System Huntington disease


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A 21-year-old man comes to the office with impaired balance, tremor, and difficulty speaking. His symptoms have developed slowly over the last several months. The patient is found to have elevated serum transaminases. Viral hepatitis serologies are negative. He does not use tobacco, alcohol, or illicit drugs. He has a sibling who was diagnosed at a young age with a progressive neurologic disease. Which of the following diagnostic studies would be the most helpful for confirming the diagnosis in this patient?

A. Anti-smooth muscle antibodies
B. Genetic testing for triplet repeat expansions
C. MRI of the brain
D. Serum alpha-1 antitrypsin level
E. Serum ferritin and transferrin saturation
F. Slit lamp examination

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A. Anti-smooth muscle antibodies (4%)
B. Genetic testing for triplet repeat expansions (28%)
C. MRI of the brain (13%)
D. Serum alpha-1 antitrypsin level (3%)
E. Serum ferritin and transferrin saturation (10%)
F. Slit lamp examination (40%)

Correct

40%
Answered correctly

01 min, 25 secs
Time Spent

01/09/2021
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| Wilson disease | |
|---|---|
| **Pathogenesis** | • Autosomal recessive mutation of *ATP7B* → hepatic copper accumulation → leak from damaged hepatocytes → deposits in tissues (eg, basal ganglia, cornea) |
| **Clinical findings** | • Hepatic (acute liver failure, chronic hepatitis, cirrhosis)<br>• Neurologic (parkinsonism, gait disturbance, dysarthria)<br>• Psychiatric (depression, personality changes, psychosis) |
| **Diagnosis** | • ↓ Ceruloplasmin & ↑ urinary copper excretion<br>• Kayser-Fleischer rings on slit-lamp |



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| | changes, psychosis) |
| **Diagnosis** | • ↓ Ceruloplasmin & ↑ urinary copper excretion<br>• Kayser-Fleischer rings on slit-lamp examination<br>• ↑ Copper content on liver biopsy |
| **Treatment** | • Chelators (eg, D-penicillamine, trientine)<br>• Zinc (interferes with copper absorption) |

**Wilson disease** is a rare, autosomal recessive disorder most often identified in individuals age 5-40. A mutation of gene *ATP7B* hinders intracellular hepatocyte copper transport, causing reduced formation/secretion of ceruloplasmin (the major extracellular copper transport protein) and **decreased secretion of copper** into the biliary system. Copper is a pro-oxidant and causes **hepatocellular injury** by producing free radicals. Eventually, copper leaks from injured hepatocytes into the blood to be deposited in various tissues (eg, basal ganglia, cornea).

Neurologic involvement can result in **movement abnormalities** and **psychiatric symptoms**. Almost all patients with neuropsychiatric disease have Kayser-Fleischer rings (green/brown copper deposits in the


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various tissues (eg, basal ganglia, cornea).

Neurologic involvement can result in **movement abnormalities** and **psychiatric symptoms**. Almost all patients with neuropsychiatric disease have Kayser-Fleischer rings (green/brown copper deposits in the Descemet membrane of the cornea), which can be detected on slit lamp examination if not seen on visual inspection. The diagnosis can be confirmed by the presence of **low serum ceruloplasmin**, increased urinary copper excretion, and elevated hepatic copper content on liver biopsy.

**(Choice A)** Anti-smooth muscle antibodies are associated with autoimmune hepatitis. Although serum transaminases can be elevated, neurologic symptoms are not characteristic.

**(Choice B)** Genetic testing for triplet repeat expansions may be considered in patients with suspected Friedreich ataxia, an autosomal recessive disorder that typically presents during adolescence with neurologic dysfunction (eg, limb/gait ataxia, dysarthria) and hypertrophic cardiomyopathy.

**(Choice C)** Although atrophy/cavitation of the basal ganglia may be identified on brain MRI in patients with advanced Wilson disease, these findings are not specific and therefore are not used to confirm the diagnosis. Neuroimaging can be useful in excluding other causes of movement disorder (eg, tumor, infarction, demyelinating disease).

**(Choice D)** Alpha-1 antitrypsin deficiency is an autosomal codominant disorder that usually presents with


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various tissues (eg, basal ganglia, cornea)

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(Choice D) Alpha-1 antitrypsin deficiency is an autosomal codominant disorder that usually presents with



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**(Choice C)** Although atrophy/cavitation of the basal ganglia may be identified on brain MRI in patients with advanced Wilson disease, these findings are not specific and therefore are not used to confirm the diagnosis. Neuroimaging can be useful in excluding other causes of movement disorder (eg, tumor, infarction, demyelinating disease).

**(Choice D)** Alpha-1 antitrypsin deficiency is an autosomal codominant disorder that usually presents with early onset (age ≤45), panacinar emphysema, and liver disease.

**(Choice E)** Elevated serum ferritin and transferrin saturation is characteristic of hemochromatosis, an autosomal recessive disorder associated with increased intestinal iron absorption. Patients typically present with liver disease, skin pigmentation, diabetes mellitus, and cardiac enlargement due to excessive iron deposition into tissues.

**Educational objective:**

Wilson disease is an autosomal recessive condition characterized by excessive copper deposition into tissues (eg, liver, basal ganglia, cornea). It typically presents in young adults with liver disease, neuropsychiatric symptoms (eg, gait disturbance, dysarthria, depression, personality changes), and Kayser-Fleischer rings on slit lamp examination.

**References**



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A 19-year-old man comes to the emergency department after being stabbed in the right arm during a fight. The patient has no chronic medical conditions. Vital signs are within normal limits. Examination of the right upper extremity shows a 4-cm laceration oriented transversely over the volar (flexor) surface of the proximal forearm. The patient is taken to the operating room for surgical repair. While exploring the wound, a nerve that courses between the flexor digitorum superficialis and profundus muscles is found to be transected. Which of the following movements is most likely to be impaired in this patient?

A. Adduction of the third and fourth digits
B. Adduction of the thumb
C. Extension of the metacarpophalangeal joints
D. Extension of the wrist
E. Opposition of the thumb
F. Supination of the forearm

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A. ~~Adduction of the third and fourth digits~~ (13%)

B. Adduction of the thumb (13%)

C. ~~Extension of the metacarpophalangeal joints~~ (5%)

D. ~~Extension of the wrist~~ (6%)

✓ E. Opposition of the thumb (49%)

F. ~~Supination of the forearm~~ (11%)



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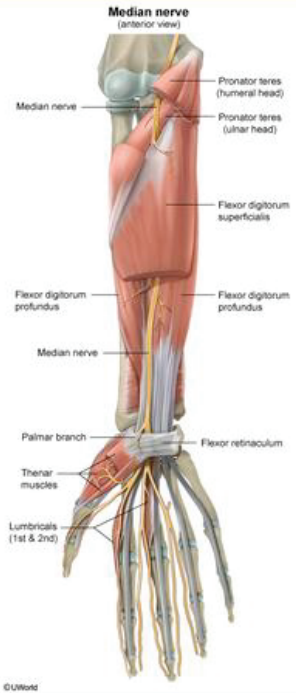


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The **median nerve** is formed from spinal nerves C5-T1 via the medial and lateral cords of the brachial plexus. It courses with the brachial artery between the biceps brachii and brachialis muscles before entering the forearm. In the anterior (volar) forearm, the median nerve passes between the heads of the pronator teres before coursing **between the flexor digitorum superficialis and profundus** muscles. It ultimately passes into the hand through the carpal tunnel beneath the flexor retinaculum.

The median nerve is most commonly injured by compression within the carpal tunnel (ie, carpal tunnel syndrome), leading to pain and numbness in the first 3 digits and lateral half of the fourth, along with **weakness of thumb flexion and opposition**. However, the nerve can be injured more proximally by penetrating trauma to the upper forearm, supracondylar fracture, or entrapment between the heads of pronator teres. In addition to the above symptoms, proximal injury causes decreased sensation over the thenar eminence and weakness of flexion in the wrist and second and third digits (ie, preacher or **benediction hand**).

**(Choices A and B)** The adductor pollicis muscle (adduction of the thumb) and palmar interossei (adduction of the third and fourth digits) are innervated by the deep branch of the ulnar nerve. The ulnar nerve courses between the flexor digitorum profundus and flexor carpi ulnaris in the medial forearm.

**(Choices C and F)** The extensor digitorum (extension of digits at metacarpophalangeal joints) and



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The **median nerve** is formed from spinal nerves C5-T1 via the medial and lateral cords of the brachial

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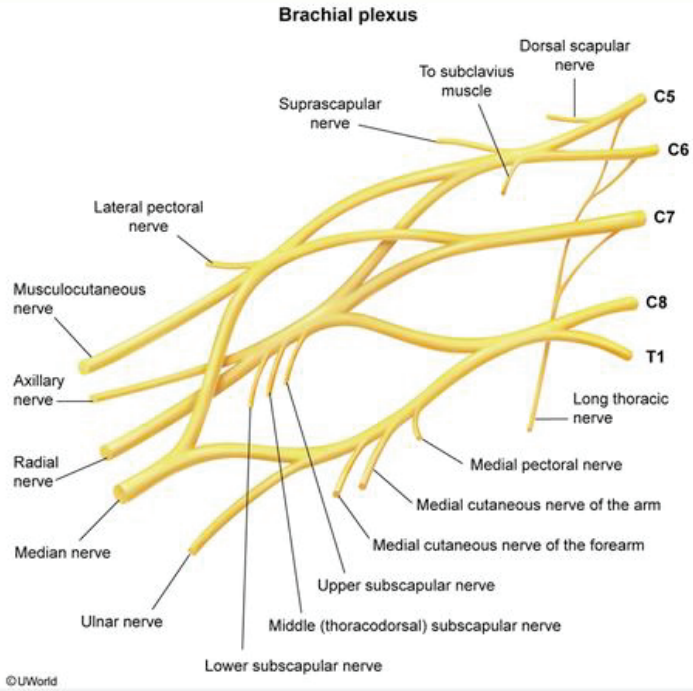


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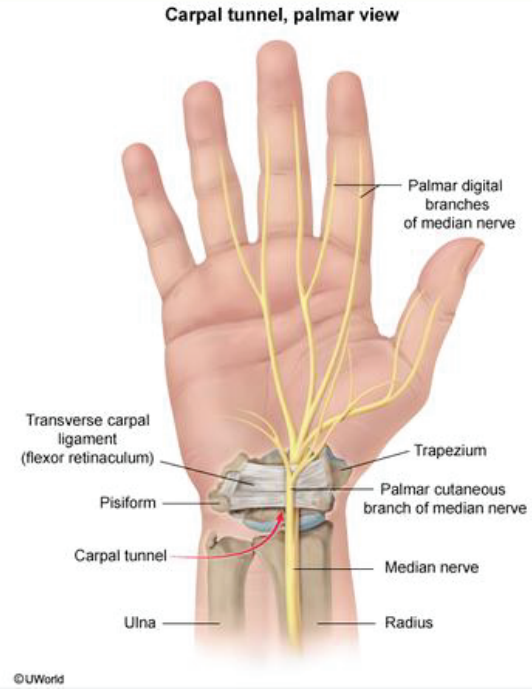


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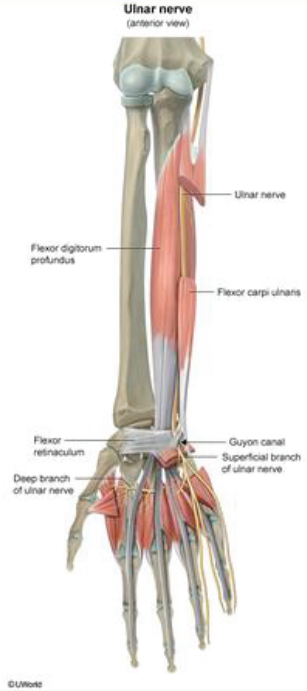


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nerve courses between the flexor digitorum profundus and flexor carpi ulnaris in the medial forearm.

**(Choices C and F)** The extensor digitorum (extension of digits at metacarpophalangeal joints) and supinator (supination of forearm) are innervated by the deep branch of the radial nerve (posterior interosseous nerve). This nerve runs in the posterior forearm between the deep and superficial extensor muscles.

**(Choice D)** Extension of the wrist is largely performed by extensor carpi ulnaris and extensor carpi radialis longus and brevis, which are innervated by the radial nerve. The radial nerve courses between the medial and lateral heads of the triceps brachii in the upper arm before splitting into deep and superficial branches.

**Educational objective:**

The median nerve is most commonly injured within the carpal tunnel, leading to pain and numbness in the first 3 digits and lateral half of the fourth, as well as weakness of thumb flexion and opposition. More proximal injury (in the forearm) additionally causes decreased sensation over the thenar eminence and weakness of flexion in the wrist and second and third digits.

**References**

- High median nerve injuries.



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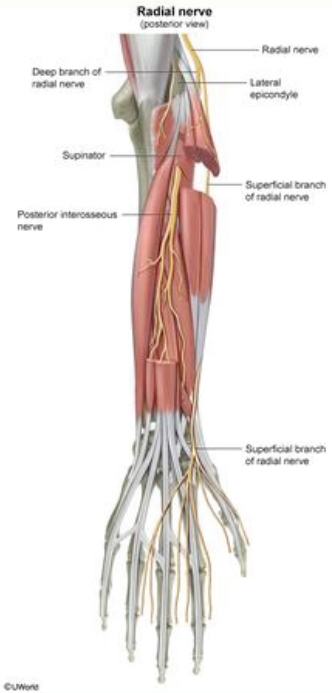


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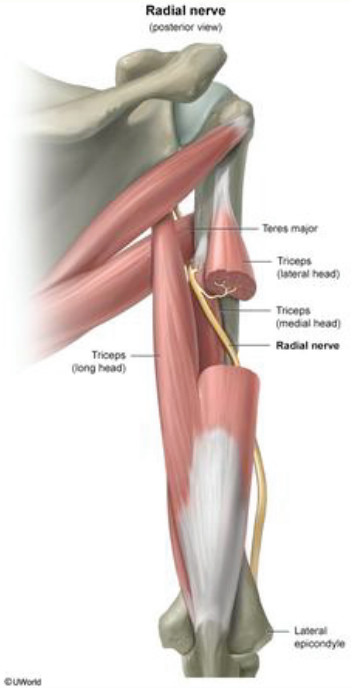


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A 75-year-old man is brought to the emergency department after he was found unresponsive at home. The patient has a history of poorly controlled hypertension. Blood pressure is 240/120 mm Hg and pulse is 104 /min. He has extensor posturing and pinpoint pupils. CT scan of the head without contrast reveals an acute pontine hemorrhage with associated mass effect. The patient dies several hours later. Autopsy reveals disruption of all pigmented neurons in the posterior rostral pons at the lateral floor of the fourth ventricle. These neurons normally produce which of the following?

A. Dopamine
B. Dynorphin
C. Epinephrine
D. Histamine
E. Norepinephrine
F. Orexin
G. Oxytocin
H. Vasopressin



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acute pontine hemorrhage with associated mass effect. The patient dies several hours later. Autopsy reveals disruption of all pigmented neurons in the posterior rostral pons at the lateral floor of the fourth ventricle. These neurons normally produce which of the following?

A. Dopamine (49%)
B. Dynorphin (6%)
C. Epinephrine (3%)
D. Histamine (1%)
✓ E. Norepinephrine (25%)
F. Orexin (8%)
G. Oxytocin (1%)
H. Vasopressin (3%)

Correct

25%
Answered correctly

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This patient had a hypertensive hemorrhage in the pons at the level of the **locus ceruleus**, a paired pigmented brainstem nucleus located in the **posterior rostral pons** near the **lateral floor of the fourth ventricle**. The locus ceruleus functions as the principal site for **norepinephrine** synthesis in the brain and projects to virtually all parts of the central nervous system. It is involved in the control of mood, **arousal** (reticular activating system), sleep-wake states, cognition, and autonomic function (eg, blood pressure control). Abnormal activation of the locus ceruleus has been implicated in the pathogenesis of anxiety disorders (eg, panic attacks).

Patients with bilateral pontine hemorrhage typically present with coma due to disruption of the **reticular activating system**. Other features usually include total paralysis with extensor posturing due to corticospinal and corticobulbar tract injury and pinpoint pupils secondary to descending sympathetic tract damage.

**(Choice A)** Dopamine is produced in the ventral tegmental area and substantia nigra pars compacta located in the midbrain. The major dopaminergic pathways in the brain include the mesolimbic and mesocortical pathways (regulate cognition and behavior), the nigrostriatal pathway (regulates coordination of voluntary movements), and the tuberoinfundibular pathway (inhibits prolactin secretion).

**(Choice B)** Dynorphin is an opioid peptide that modulates the pain response. It is produced mostly in the


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**(Choice B)** Dynorphin is an opioid peptide that modulates the pain response. It is produced mostly in the


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**(Choice B)** Dynorphin is an opioid peptide that modulates the pain response. It is produced mostly in the periaqueductal gray, rostral ventral medulla, and dorsal horn of the spinal cord.

**(Choice C)** Norepinephrine is converted to epinephrine primarily in the adrenal medullae. Both of these neurotransmitters are released by the adrenal glands into the circulation after stimulation by sympathetic cholinergic preganglionic neurons.

**(Choices D and F)** Histamine and orexin are produced in the posterior hypothalamus and play an important role in arousal and wakefulness.

**(Choices G and H)** Oxytocin and vasopressin (antidiuretic hormone) are hormones produced by the hypothalamus and released from the posterior pituitary. Oxytocin promotes milk letdown and uterine contractions, whereas vasopressin causes vasoconstriction and free water reabsorption in the renal collecting ducts.

**Educational objective:**
The locus ceruleus is a paired brainstem nucleus located in the posterior rostral pons near the lateral floor of the fourth ventricle and functions as the principal site for norepinephrine synthesis in the brain. It projects to virtually all parts of the central nervous system and helps control mood, arousal (reticular activating system), sleep-wake states, cognition, and autonomic function.



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A 22-year-old woman comes to the emergency department due to acute vision disturbances and headache. About an hour ago the patient experienced a small area of visual loss, which she describes as a hole in the visual field. The vision disturbance gradually expanded to a C-shape in her peripheral vision and spontaneously resolved after 15-20 minutes. A progressively worsening, severe, right-sided headache of pulsating quality quickly followed. The patient has had similar headaches in the past but not of such severity. She has no other medical conditions and takes no medications. Blood pressure is 150/86 mm Hg and pulse is 92/min. On physical examination, the patient is lying still in bed with eyes closed. The pupils are equal and reactive to light. Funduscopic examination reveals no abnormalities. Bilateral upper and lower extremity muscle strength, deep tendon reflexes, and sensation are normal. Which of the following is the most likely diagnosis?

A. Acute angle-closure glaucoma
B. Cluster headache
C. Migraine with aura
D. Optic neuritis
E. Simple partial seizure



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A. Acute angle-closure glaucoma
B. Cluster headache
C. Migraine with aura
D. Optic neuritis
E. Simple partial seizure
F. Transient ischemic attack

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- A. Acute angle-closure glaucoma (3%)
- ✗ B. Cluster headache (6%)
- ✓ C. Migraine with aura (73%)
- D. Optic neuritis (6%)
- E. Simple partial seizure (0%)
- F. Transient ischemic attack (9%)

Incorrect



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This young woman with a pulsating, unilateral headache preceded by visual field loss has **migraine with aura**. Migraines are an episodic neurological disorder that results in severe, **unilateral**, **throbbing headaches** often associated with photophobia, phonophobia, and nausea/vomiting. Migraines typically last 4-72 hours and have a strong genetic predisposition; **women** are affected more frequently than men.

Migraines are thought to be triggered by a self-propagating wave of depolarization spreading across neurons in the cerebral cortex, resulting in activation and sensitization of trigeminal nerve nociceptors. Up to 25% of patients also develop **focal**, **reversible neurologic symptoms** that precede or accompany the headache, known as an **aura**. Auras may be due to the spread of depolarization into other areas of the brain, where they are interpreted as "positive" (eg, bright spots, noises, paresthesia, movements) or "negative" (eg, vision/hearing/sensation loss) symptoms. Auras typically develop progressively over a period of minutes.

**(Choice A)** Acute angle-closure glaucoma causes headache and decreased vision associated with elevated intraocular pressures. However, patients are typically older (age >60), and severe eye pain and conjunctival erythema are common. Vision would not be expected to improve without intervention.

**(Choice B)** Cluster headache causes severe unilateral headaches; however, ipsilateral autonomic


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conjunctival erythema are common. Vision would not be expected to improve without intervention.

**(Choice B)** Cluster headache causes severe unilateral headaches; however, ipsilateral autonomic symptoms (eg, lacrimation, rhinorrhea, flushing, diaphoresis) are expected. The disease is also more common in men and is not associated with aura.

**(Choice D)** Optic neuritis is a demyelinating disorder that causes vision loss, but it is typically unilateral and progresses over a period of weeks. Patients have eye pain that is worse with movement, color vision is often affected, and an afferent pupillary defect is present.

**(Choice E)** Simple partial seizure may be preceded by an aura, but seizures typically cause positive symptoms (eg, lip smacking, arm movement, seeing bright lights) rather than the negative symptoms seen in this patient, and typically last <2 minutes. Unilateral headache is more suggestive of migraine with aura.

**(Choice F)** Transient ischemic attacks (TIAs) also cause focal neurologic deficits; however, these typically have an acute onset, with maximal symptoms at onset rather than the progressive visual field deficit seen in this patient. In addition, TIAs typically occur in older patients with vascular risk factors (eg, smoking, hyperlipidemia) and would be very uncommon in an otherwise healthy young woman.

**Educational objective:**


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**Educational objective:**
Migraines are an episodic neurological disorder that results in severe, unilateral, throbbing headaches often associated with photophobia, phonophobia, and nausea/vomiting. Migraines typically last 4-72 hours, and up to 25% of patients also develop an aura (focal, reversible neurologic symptoms that precede or accompany the headache).

| Pathology | Nervous System | Migraine |
|---|---|---|
| Subject | System | Topic |


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A 70-year-old man comes to the physician with muscle rigidity that impairs his daily activities. He was diagnosed with Parkinson disease 5 years ago and takes levodopa/carbidopa. His initial response to the medication allowed him to continue all of his usual activities. Recently, the patient has been experiencing episodes of sudden restricted mobility lasting several hours, and sometimes he "freezes" altogether. These episodes alternate with symptom-free periods in which he is mobile and feels well. The patient desires relief as he believes he can still "do so much" with his life. During discussion of this patient's fluctuating mobility, which of the following should the physician emphasize?

A. Drug holidays are helpful
B. Drug response is unpredictable
C. Fluctuations are caused by enhanced drug metabolism
D. Fluctuations are temporary and will resolve spontaneously
E. Stopping carbidopa is the best management

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A. Drug holidays are helpful (22%)
B. Drug response is unpredictable (35%)
C. Fluctuations are caused by enhanced drug metabolism (26%)
D. Fluctuations are temporary and will resolve spontaneously (10%)
E. Stopping carbidopa is the best management (5%)



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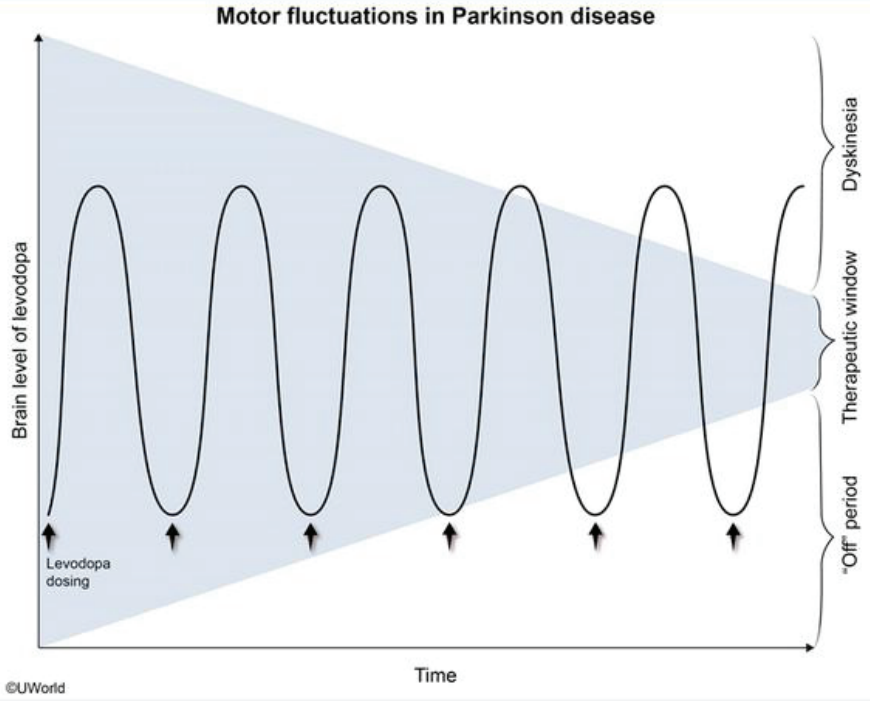


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Long-term treatment of **Parkinson disease** (PD) with **levodopa** can be complicated by periodic fluctuations in motor function: patients have good mobility during "on" periods and increased bradykinesia/rigidity during "off" periods (**"on-off" phenomenon**). Oftentimes, these fluctuations appear to correlate with serum drug levels (eg, reduced mobility 4 hours after the last dose). As PD progresses, the therapeutic window for levodopa narrows, possibly due to natural or levodopa-induced **nigrostriatal degeneration**. As a result, small changes in serum drug levels can result in motor fluctuations (eg, mild elevations may result in dyskinesia, whereas slight reductions may result in bradykinesia/rigidity). In advanced PD, motor fluctuations can occur independently of medication dosing and may become unpredictable.

**(Choice A)** Drug holidays have not been shown to be effective in preventing motor fluctuations in PD. Also, stopping levodopa abruptly is not recommended as it could cause a condition similar to neuroleptic malignant syndrome.

**(Choices C and D)** Progressive nigrostriatal neurodegeneration, not enhanced drug metabolism, is thought to be responsible for motor fluctuations in PD. As such, motor fluctuations are not typically temporary or self-limiting and usually require long-term medical management.

**(Choice E)** Discontinuation of carbidopa (a decarboxylase inhibitor) is inappropriate as carbidopa reduces


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**(Choices C and D)** Progressive nigrostriatal neurodegeneration, not enhanced drug metabolism, is thought to be responsible for motor fluctuations in PD. As such, motor fluctuations are not typically temporary or self-limiting and usually require long-term medical management.

**(Choice E)** Discontinuation of carbidopa (a decarboxylase inhibitor) is inappropriate as carbidopa reduces the peripheral conversion of levodopa to dopamine and consequently minimizes systemic side effects (eg, nausea/vomiting).

**Educational objective:**

Long-term treatment of Parkinson disease with levodopa can be complicated by periodic and sometimes unpredictable fluctuations in motor function. This "on-off" phenomenon is thought to be a consequence of progressive nigrostriatal neurodegeneration leading to a decreased therapeutic window for levodopa.

**References**

- Treatment of motor symptoms in advanced Parkinson's disease: a practical approach.

| Pharmacology | Nervous System | Parkinson disease |
|---|---|---|
| Subject | System | Topic |

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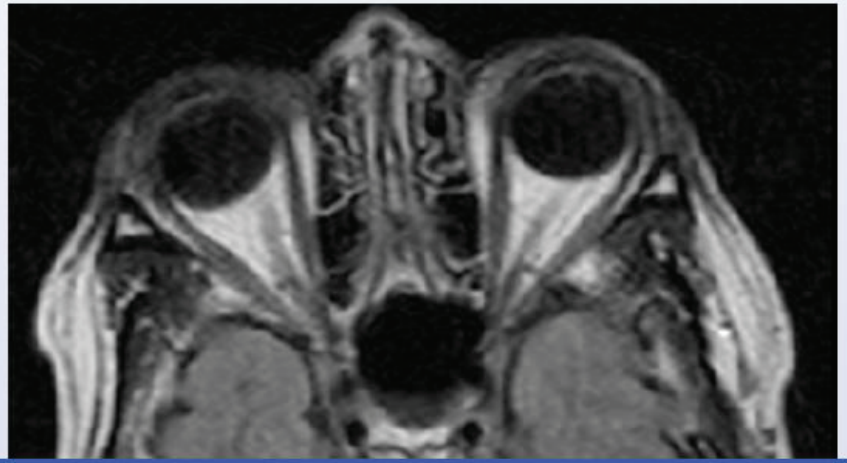
A 65-year-old man comes to the emergency department due to acute-onset slurred speech. He also has right-sided weakness but denies any trauma, headache, or loss of consciousness. His medical problems include hypertension and type 2 diabetes mellitus. The patient has smoked 1 pack of cigarettes daily for 20 years. Neurologic examination shows right-sided lower facial droop with sparing of the forehead muscles. Motor strength is 3/5 on the right and 5/5 on the left with a Babinski response on the right. There is also dysmetria and dysdiadochokinesia involving his right upper and lower extremities. MRI of the brain reveals an acute lacunar infarct in the brainstem, as shown in the image below.





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Item 2 of 11
Question Id: 2125

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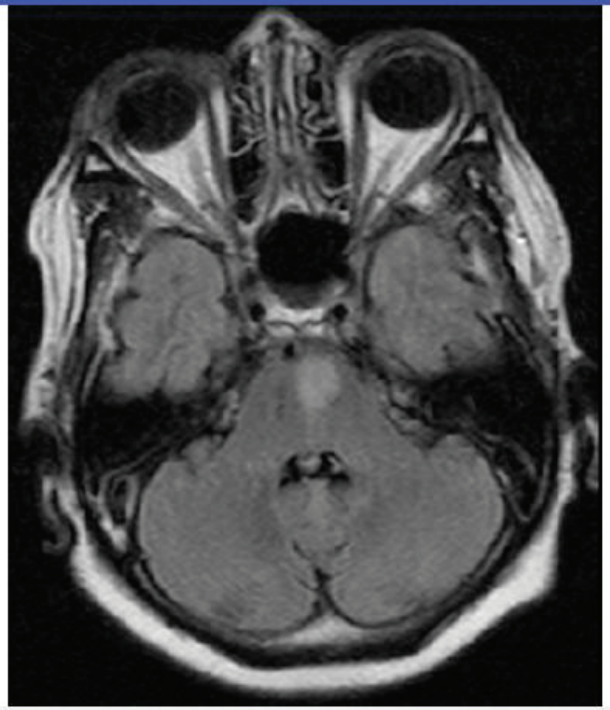

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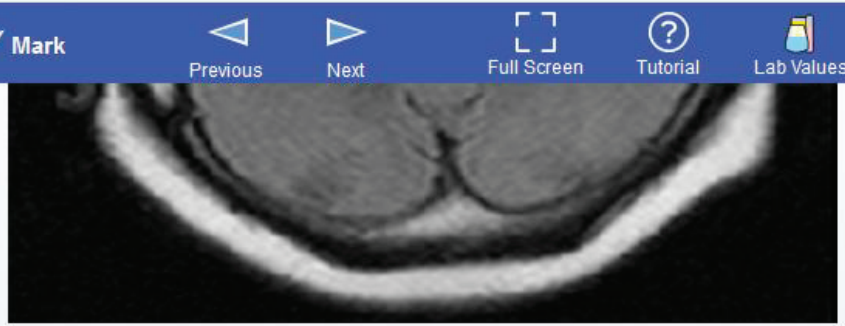

Which of the following cranial nerves exits the brainstem closest to the level affected by this patient's stroke?

- A. Facial
- B. Hypoglossal
- C. Oculomotor
- D. Trigeminal
- E. Trochlear

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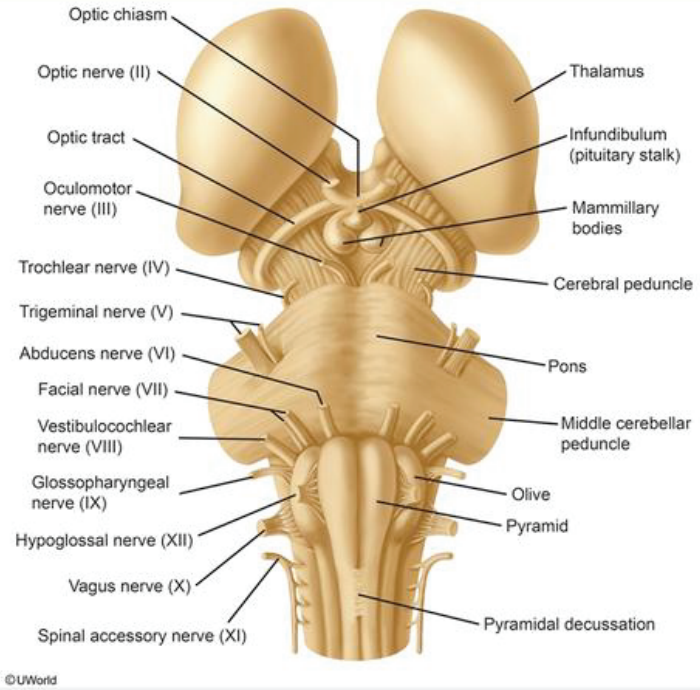


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This patient has an acute lacunar ischemic stroke affecting the left medial pons at the level of the middle cerebellar peduncle. The **trigeminal nerve** (CN V) exits the brainstem at the lateral aspect of the **mid-pons** at the level of the **middle cerebellar peduncles** (a key neuroanatomic landmark for locating the nerve). The trigeminal sensory nuclei (eg, principal sensory, spinal, mesencephalic) run from the midbrain to the upper cervical spine and receive afferent signals for facial sensation via all 3 nerve branches (ophthalmic, maxillary, and mandibular). The motor nucleus is located in the lateral mid-pons and sends efferent signals to the muscles of mastication (eg, temporalis, masseter, pterygoids) via the mandibular branch.

**Infarcts** involving the **anterior pons** can affect the corticospinal tract (**contralateral hemiparesis**, Babinski sign) and corticobulbar tract (contralateral **lower facial palsy**, dysarthria). Disruption of the corticopontine fibers that convey motor information from the cortex to the ipsilateral pontine gray matter may also result in contralateral dysmetria and dysdiadochokinesia (**ataxic hemiparesis**). The cerebellar deficits are contralateral to the lesion as the pontocerebellar fibers arising from the pontine gray matter decussate and enter the cerebellum through the contralateral middle cerebellar peduncle.

**(Choice A)** The facial nucleus is located in the dorsolateral aspect of the caudal pons, and the nerve exits at the ventrolateral pontomedullary junction (below the middle cerebellar peduncles). This patient has sparing of the forehead muscles, which indicates that his facial weakness is a result of a central lesion


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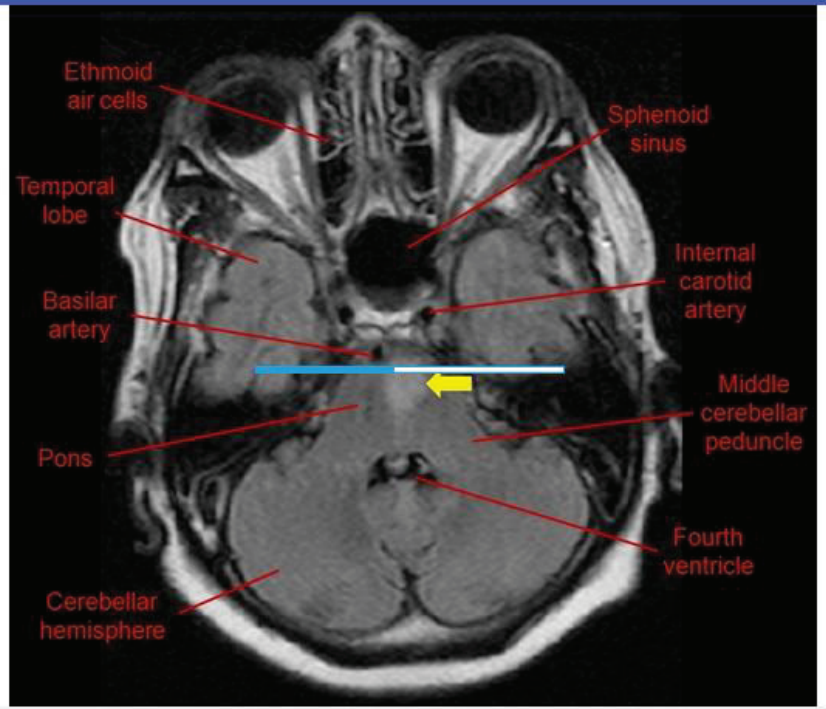


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**(Choice A)** The facial nucleus is located in the dorsolateral aspect of the caudal pons, and the nerve exits at the ventrolateral pontomedullary junction (below the middle cerebellar peduncles). This patient has **sparing** of the forehead muscles, which indicates that his facial weakness is a result of a central lesion affecting the corticobulbar tract and is not due to direct damage to the facial nucleus/nerve.

**(Choice B)** The hypoglossal nucleus is located medially on the floor of the fourth ventricle at the level of the medulla, and the nerve exits at the rostral end of the preolivary sulcus.

**(Choice C)** The oculomotor nucleus is located in the rostral midbrain at the level of the superior colliculus and red nucleus, and the nerve exits at the interpeduncular fossa.

**(Choice E)** The trochlear nucleus is located in the caudal midbrain, and the nerve exits the dorsal midbrain just below the inferior colliculus (below the red nucleus). The trochlear nerve is the only cranial nerve to decussate before innervating its target (superior oblique muscle).

**Educational objective:**
Infarcts involving the anterior portion of the medial pons can produce dysarthria and contralateral hemiparesis/lower facial palsy due to disruption of the ipsilateral corticospinal and corticobulbar tracts. The trigeminal nerve arises at the level of the middle cerebellar peduncle at the lateral aspect of the mid-pons.


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A researcher is studying neuronal changes in various physiologic and pathologic states. Microscopic examination of neural tissue obtained from experimental animals reveals neurons with shrunken nuclei and eosinophilic cytoplasm lacking Nissl bodies. Which of the following is the most likely cause of these findings?

A. Accumulation of abnormal proteins
B. Age-related physiologic changes
C. Defective lysosomal autophagy
D. Irreversible ischemic injury
E. Transection injury of the nerve fiber
F. Transient neural compression

Submit



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A. Accumulation of abnormal proteins (4%)
B. Age-related physiologic changes (5%)
C. Defective lysosomal autophagy (2%)
✓ D. Irreversible ischemic injury (66%)
E. Transection injury of the nerve fiber (19%)
F. Transient neural compression (1%)

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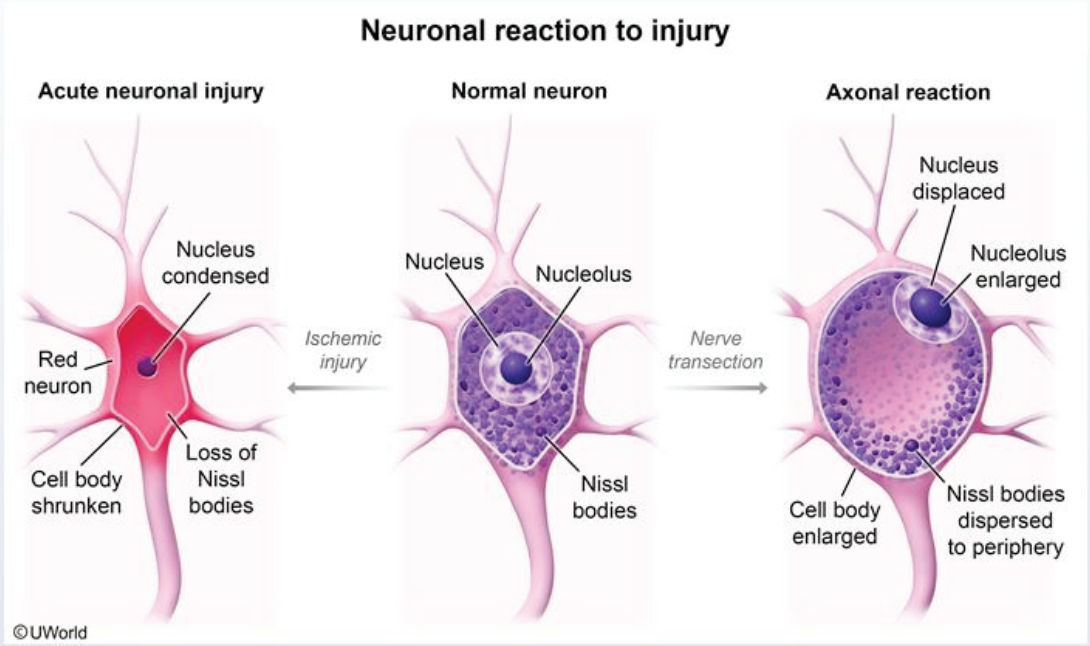


Neurons are the major functional unit of the nervous system and are characterized histologically by large, round, centrally located nuclei and basophilic cytoplasmic granules composed of rough endoplasmic


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Neurons are the major functional unit of the nervous system and are characterized histologically by large, round, centrally located nuclei and basophilic cytoplasmic granules composed of rough endoplasmic reticulum (Nissl bodies). When neurons are injured, they undergo distinct histopathologic changes depending on the type of underlying injury.

In response to an **acute irreversible injury** (eg, severe hypoglycemia, **ischemia**), neurons begin to display characteristic morphologic changes 12-24 hours after the inciting event, appearing as shrunken cells separated from the surrounding tissue. The **nucleus** becomes **pyknotic** (shrunken and basophilic with loss of the nucleolus), and the basophilic **Nissl bodies disappear**, resulting in cytoplasm that stains deeply eosinophilic **(red neurons)**.

In the brain, in contrast to most other tissues, ischemia ultimately results in liquefactive necrosis due to the breakdown of neural architecture by hydrolytic enzymes released from reacting inflammatory cells and damaged neurons. The necrotic neuronal remnants are then phagocytized by microglia, and astrocytes proliferate at the site of the injury to form a glial scar.

**(Choice A)** Several neurodegenerative diseases (eg, Alzheimer disease, frontotemporal lobar degeneration) are characterized by intracellular and/or extracellular accumulation of abnormal proteins in neural tissue. Histologic examination of affected areas demonstrates proteinaceous plaques, tangles,


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**(Choice A)** Severa
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| Type of response | Type of injury | Histopathologic changes |
|---|---|---|
| **Acute neuronal injury** | • Severe insult (eg, ischemia) leading to cell death | • Shrinkage of the cell body<br>• Pyknosis of the nucleus<br>• Loss of Nissl bodies<br>• Eosinophilic cytoplasm (red neuron) |
| **Axonal reaction (regeneration)** | • Axon transection | • Enlargement of the cell body<br>• Eccentrically placed nucleus<br>• Enlargement of the nucleolus<br>• Dispersion of Nissl bodies |
| **Chronic neuronal injury** | • Progressive degenerative disease (eg, ALS, Parkinson disease) | • Loss of functionally related neurons<br>• Reactive gliosis |

ALS = amyotrophic lateral sclerosis.

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**(Choice A)** Several neurodegenerative diseases (eg, Alzheimer disease, frontotemporal lobar degeneration) are characterized by intracellular and/or extracellular accumulation of abnormal proteins in neural tissue. Histologic examination of affected areas demonstrates proteinaceous plaques, tangles, and/or inclusions with reactive gliosis and loss of neurons.

**(Choice B)** Normal aging is associated with progressive atrophy and neuronal loss. However, red neuron changes are not characteristic of age-related physiologic changes.

**(Choice C)** Lysosomal storage diseases (eg, Tay-Sachs, Niemann-Pick) cause the accumulation of improperly digested substances in lysosomes, leading to neural degeneration through free radical damage and apoptosis. Expected histopathologic changes include enlarged neuronal cells with a foamy appearance due to accumulated undigested macromolecules.

**(Choice E)** Extensive axon damage or transection results in an axonal reaction characterized by cell body swelling, movement of the nucleus to the periphery, and dispersion of Nissl bodies. This response occurs due to increased protein and lipid synthesis during axon regeneration.

**(Choice F)** Transient neural compression can lead to a temporary loss of function due to ischemia but would not lead to significant histopathologic changes unless the compression was sustained. Neural compression may occur in the CNS due to increased intracranial pressure or a mass lesion.


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(Choice A) Several neurodegenerative diseases (eg, Alzheimer disease, frontotemporal lobar

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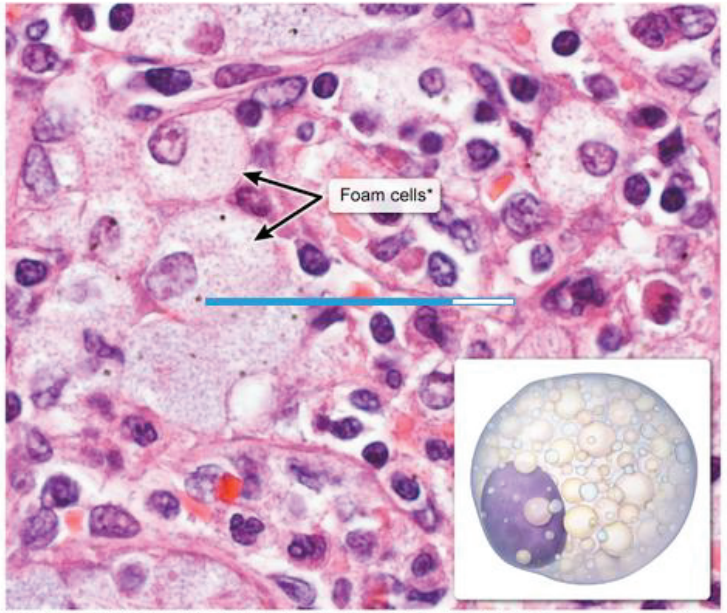
Niemann-Pick disease




*Macrophages with foamy cytoplasm due to sphingomyelin accumulation in lysosomes.

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**Educational objective:**

Neurons that sustain irreversible ischemic injury begin to develop characteristic histopathologic changes 12-24 hours after the inciting event. These changes include shrinkage of the cell body, pyknosis of the nucleus, loss of Nissl bodies, and cytoplasmic eosinophilia (red neurons).

| Pathology | Nervous System | Ischemic stroke |
|---|---|---|
| Subject | System | Topic |

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A 12-year-old boy is evaluated for chronic headaches and visual changes. The headaches have progressively worsened over the past year and are associated with nausea. The patient's parents are especially concerned as his symptoms have been interfering with his coursework in middle school. An intracranial calcified mass is detected on brain imaging. The mass is surgically removed and on gross inspection shows cystic spaces filled with thick, brownish-yellow fluid that is rich in cholesterol. This mass is most likely derived from cells responsible for forming which of the following structures?

A. Anterior pituitary
B. Cerebellar vermis
C. Choroid plexus
D. Pineal gland
E. Retina

Submit



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A 12-year-old boy is evaluated for chronic headaches and visual changes. The headaches have progressively worsened over the past year and are associated with nausea. The patient's parents are especially concerned as his symptoms have been interfering with his coursework in middle school. An intracranial calcified mass is detected on brain imaging. The mass is surgically removed and on gross inspection shows cystic spaces filled with thick, brownish-yellow fluid that is rich in cholesterol. This mass is most likely derived from cells responsible for forming which of the following structures?

- A. Anterior pituitary (59%)
- B. ~~Cerebellar vermis~~ (5%)
- C. ~~Choroid plexus~~ (13%)
- D. ~~Pineal gland~~ (17%)
- E. Retina (4%)

Correct

59%
Answered correctly

01 min, 09 secs
Time Spent

12/29/2020
Last Updated



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## Explanation

**Pituitary embryology**

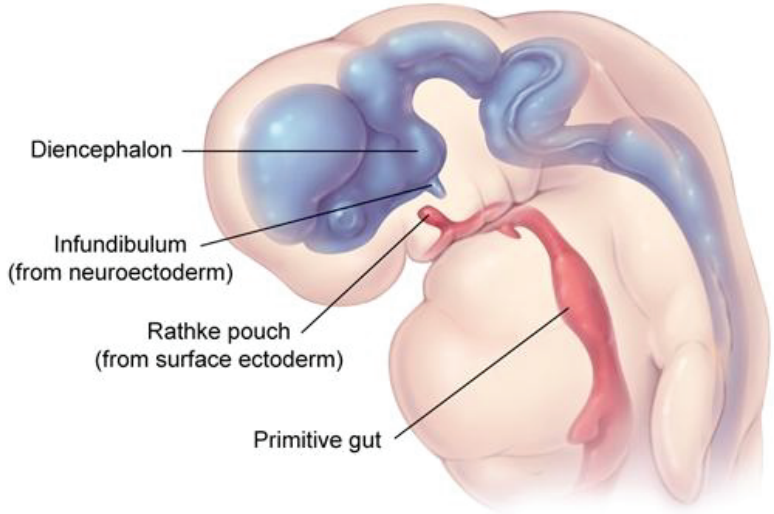




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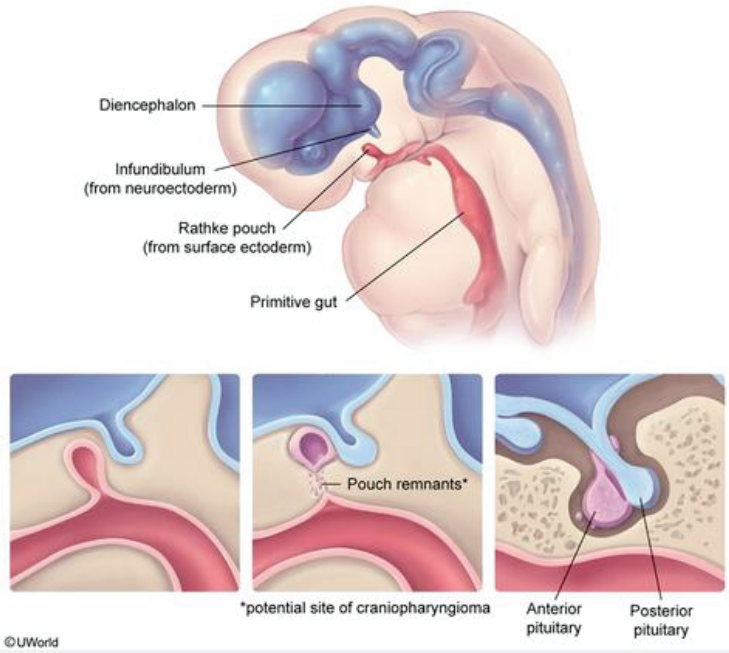
Exhibit Display

Pituitary embryology

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This patient most likely has an adamantinomatous **craniopharyngioma**. These are rare, slow-growing (benign) intracranial tumors found in children and typically located in the suprasellar region. On macroscopic examination, they are **cystic** or partially cystic with solid areas. The cysts are usually filled with a brownish-yellow, viscous fluid that resembles machine oil due to the presence of protein and **cholesterol crystals**. Dystrophic **calcification** of the cysts is highly characteristic and may be detected on neuroimaging. On light microscopy, the cysts are lined by cords/nests of stratified squamous epithelium with peripheral palisading and internal areas of lamellar "wet" keratin.

Craniopharyngiomas are derived from remnants of **Rathke's pouch**, which is an evagination of the surface ectoderm that lines the fetal oral cavity. This protrusion of the roof of the mouth forms the **anterior pituitary** gland (adenohypophysis). The posterior lobe of the pituitary (neurohypophysis) forms from an outpouching of the diencephalon (infundibulum) and is derived from neuroectoderm.

**(Choices B, C, D, and E)** The cerebellum, pineal gland, and retina are derived from neuroectoderm. Epithelial cells of the choroid plexus are also derived from neuroectoderm, whereas the mesenchyme (eg, blood vessels, connective tissue) is derived from mesoderm.

**Educational objective:**

Craniopharyngiomas are suprasellar tumors found in children and composed of calcified cysts containing



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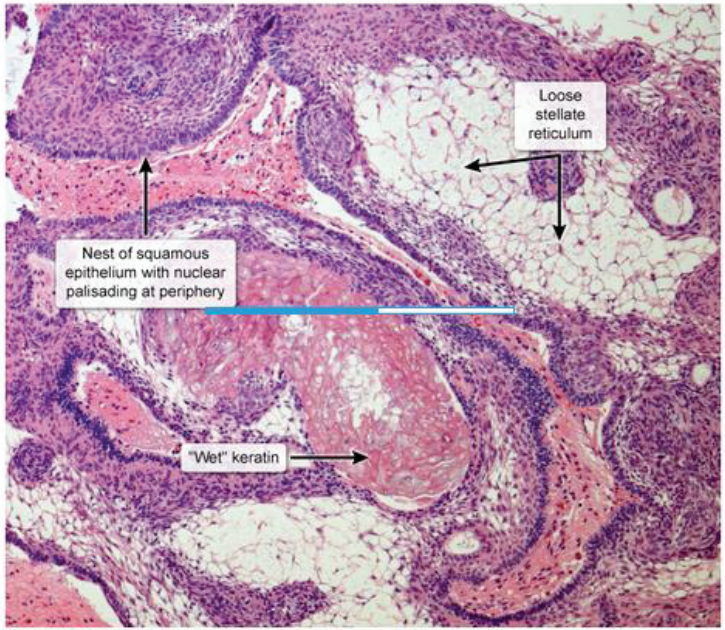
Exhibit Display

Adamantinomatous craniopharyngioma

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Craniopharyngiomas are suprasellar tumors found in children and composed of calcified cysts containing



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with a brownish-yellow, viscous fluid that resembles machine oil due to the presence of protein and **cholesterol crystals**. Dystrophic **calcification** of the cysts is highly characteristic and may be detected on neuroimaging. On light microscopy, the cysts are lined by cords/nests of stratified squamous epithelium with peripheral palisading and internal areas of lamellar "wet" keratin.

Craniopharyngiomas are derived from remnants of **Rathke's pouch**, which is an evagination of the surface ectoderm that lines the fetal oral cavity. This protrusion of the roof of the mouth forms the **anterior pituitary** gland (adenohypophysis). The posterior lobe of the pituitary (neurohypophysis) forms from an outpouching of the diencephalon (infundibulum) and is derived from neuroectoderm.

**(Choices B, C, D, and E)** The cerebellum, pineal gland, and retina are derived from neuroectoderm. Epithelial cells of the choroid plexus are also derived from neuroectoderm, whereas the mesenchyme (eg, blood vessels, connective tissue) is derived from mesoderm.

**Educational objective:**
Craniopharyngiomas are suprasellar tumors found in children and composed of calcified cysts containing cholesterol crystals. They arise from remnants of Rathke's pouch, an embryonic precursor of the anterior pituitary.

**References**



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A 21-year-old Caucasian male suffers from weakness and gait disturbance. He noticed that he has had difficulty releasing the doorknob lately. Physical examination shows cataracts, frontal baldness, and gonadal atrophy. Biopsy shows muscle atrophy involving mostly type 1 fibers. The patient's condition is best described as which of the following?

A. Denervation muscle atrophy
B. Myotonic dystrophy
C. Inflammatory myopathy
D. Ion channel myopathy
E. Myasthenia gravis
F. Oxidative phosphorylation disease

Submit



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A 21-year-old Caucasian male suffers from weakness and gait disturbance. He noticed that he has had difficulty releasing the doorknob lately. Physical examination shows cataracts, frontal baldness, and gonadal atrophy. Biopsy shows muscle atrophy involving mostly type 1 fibers. The patient's condition is best described as which of the following?

A. ~~Denervation muscle atrophy~~ (8%)
✓ B. Myotonic dystrophy (58%)
C. ~~Inflammatory myopathy~~ (5%)
D. ~~Ion channel myopathy~~ (6%)
E. ~~Myasthenia gravis~~ (4%)
✗ F. Oxidative phosphorylation disease (16%)

Incorrect
Correct answer
B

58%
Answered correctly

01 min, 53 secs
Time Spent

01/30/2021
Last Updated



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Abnormally slow relaxation of muscles is called myotonia. Classic symptoms of myotonic muscular dystrophy are difficulty loosening one's grip after a handshake or inability to release the doorknob. Myotonic muscular dystrophy is the second most common inherited muscle disorder (Duchenne muscle dystrophy is the most common).

Myotonic dystrophy is inherited as an autosomal dominant trait. It occurs because of an abnormal trinucleotide repeat expansion (CTG) of the gene that codes for a myotonia-protein kinase. The number of repeats increases with subsequent generation, causing increasingly severe disease in each generation (anticipation).

Age of presentation varies from early childhood to late adulthood. Skeletal muscle involvement includes myotonia (sustained muscle contraction). Cataracts are seen in almost all patients—frontal balding and gonadal atrophy are other common features.

On light microscopy, atrophy of muscle fibers is prominent. Type 1 fibers are more affected. Unlike Duchenne muscular dystrophy, necrosis of muscle fibers and fibrofatty replacement are not common in myotonic dystrophy.

**(Choice A)** Denervation muscle atrophy is caused by axonal destruction. It occurs due to trauma, ischemia, or generalized disease (such as amyotrophic lateral sclerosis). Clinically, denervation leads to


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myotonic dystrophy.

**(Choice A)** Denervation muscle atrophy is caused by axonal destruction. It occurs due to trauma, ischemia, or generalized disease (such as amyotrophic lateral sclerosis). Clinically, denervation leads to muscle paralysis and atrophy.

**(Choice C)** Dermatomyositis and polymyositis are examples of inflammatory myopathies.

**(Choice D)** Ion channel myopathies manifest with myotonia and episodes of hypotonic paralysis (often associated with exercise). No muscle atrophy is seen on light microscopy. PAS-positive intracytoplasmic vacuoles are found in these conditions.

**(Choices E and F)** Neither myasthenia gravis, nor mitochondrial myopathies lead to myotonia with preferential atrophy of type 1 fibers.

**Educational Objective:**
Myotonic dystrophy is an autosomal-dominant disorder. It is caused by an increased number of trinucleotide repeats on myotonia-protein kinase gene. Sustained muscle contraction (myotonia), along with weakness and atrophy, is common. Cataracts are seen in almost all patients. Frontal balding and gonadal atrophy are other common features.


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A 64-year-old Caucasian female presents to your office with headache followed by sudden onset of blindness in her right eye. She was recently admitted to the hospital for fever, pelvic and shoulder girdle pain and weight loss. This patient's condition is most likely caused by:

- A. Carotid artery atherosclerosis
- B. Cardiac embolism
- C. Hypoxic encephalopathy
- D. Hypertensive encephalopathy
- E. Large vessel arteritis
- F. Hypertensive arteriolar sclerosis
- G. Cerebral amyloid angiopathy
- H. Arteriovenous malformation
- I. Saccular aneurysm
- J. Charcot-Bouchard aneurysm



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pain and weight loss. This patient's condition is most likely caused by:

- A. Carotid artery atherosclerosis (3%)
- B. Cardiac embolism (7%)
- C. Hypoxic encephalopathy (1%)
- D. Hypertensive encephalopathy (2%)
- ✓ E. Large vessel arteritis (67%)
- F. Hypertensive arteriolar sclerosis (3%)
- G. Cerebral amyloid angiopathy (3%)
- H. Arteriovenous malformation (1%)
- I. Saccular aneurysm (4%)
- J. Charcot-Bouchard aneurysm (4%)

Correct

67%

01 min, 19 secs

01/30/2021



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**Temporal arteritis** is an inflammatory condition that affects the walls of medium-sized and large arteries. On light microscopic exam, granulomas are seen in the media of the arteries, consisting of mononuclear infiltrates and multinucleated giant cells. Due to the characteristic histologic features, this condition is also called **giant cell vasculitis**. The changes in the arteries are segmental: abnormal areas are interspersed by segments of normal-appearing arterial wall. Affected segments cause narrowing of the vessel with a decrease in blood supply to the perfused areas.

The median age of onset of the temporal arteritis is 65 years. Commonly reported symptoms include:

1. Headache: Focal pain over the temple and tenderness on palpation may be present. Sometimes patients have scalp tenderness with hair combing. Superficial temporal artery inflammation may cause pain, nodularity, and thickening found on palpation of the temporal area.
2. Craniofacial pain syndromes: Jaw claudication, tongue claudication, and facial pain may occur. This tends to appear during mastication (chewing) when the blood supply to the corresponding areas does not increase normally due to the narrowing of the arterial lumens.
3. Polymyalgia rheumatica occurs in more than half of patients with temporal arteritis. It is characterized by neck, torso, shoulder, and pelvic girdle pain and morning stiffness. Fatigue, fever, and weight loss may also occur.


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2. Craniofacial pain syndromes: Jaw claudication, tongue claudication, and facial pain may occur. This tends to appear during mastication (chewing) when the blood supply to the corresponding areas does not increase normally due to the narrowing of the arterial lumens.
3. Polymyalgia rheumatica occurs in more than half of patients with temporal arteritis. It is characterized by neck, torso, shoulder, and pelvic girdle pain and morning stiffness. Fatigue, fever, and weight loss may also occur.
4. Sudden vision loss is a dreaded complication of temporal arteritis. It may be transient or may result in permanent blindness.

**Educational Objective:**

Polymyalgia rheumatica occurs in more than half of patients with temporal arteritis. It is characterized by neck, torso, shoulder, and pelvic girdle pain and morning stiffness. Fatigue, fever and weight loss may also occur. Monocular vision loss is a common complication of temporal arteritis.

| Pathology | Nervous System | Giant cell arteritis |
|---|---|---|
| Subject | System | Topic |

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A 66-year-old man comes to the emergency department due to dizziness, dysarthria, and bilateral limb ataxia. His symptoms have been steadily worsening over the last 2 weeks. He has no other medical problems and takes no medications. He has a 50-pack-year smoking history and does not use alcohol or illicit drugs. Chest x-ray shows a mass in his right lung. He is admitted to the hospital for evaluation, but his neurologic symptoms continue to progress. He dies several months later despite receiving appropriate treatment. Autopsy shows extensive cerebellar Purkinje cell degeneration. Which of the following best describes the etiology of this patient's neurologic condition?

- A. Autoimmune
- B. Endocrine
- C. Infectious
- D. Metastatic
- E. Toxic
- F. Vascular



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ataxia. His symptoms have been steadily worsening over the last 2 weeks. He has no other medical problems and takes no medications. He has a 50-pack-year smoking history and does not use alcohol or illicit drugs. Chest x-ray shows a mass in his right lung. He is admitted to the hospital for evaluation, but his neurologic symptoms continue to progress. He dies several months later despite receiving appropriate treatment. Autopsy shows extensive cerebellar Purkinje cell degeneration. Which of the following best describes the etiology of this patient's neurologic condition?

- A. Autoimmune (20%)
- B. Endocrine (7%)
- C. ~~Infectious~~ (6%)
- D. ~~Metastatic~~ (39%)
- E. ~~Toxic~~ (3%)
- F. ~~Vascular~~ (22%)

Correct

20%
Answered correctly

02 mins, 40 secs
Time Spent

01/02/2021
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Exhibit Display

**Features of common paraneoplastic syndromes**

| Clinical presentation | Frequently associated neoplasms | Etiology |
|---|---|---|
| **Cushing syndrome** | • Small cell lung cancer<br>• Pancreatic cancer | Ectopic production of adrenocorticotropic hormone/ corticotropin-releasing hormone |
| **Syndrome of inappropriate antidiuretic hormone secretion** | • Small cell lung cancer | Ectopic vasopressin production |
| **Subacute cerebellar degeneration** | • Small cell lung cancer<br>• Breast, ovarian & uterine cancer | Anti-Yo, anti-P/Q & anti-Hu antibodies |
| **Lambert–Eaton myasthenic syndrome** | • Small cell lung cancer | Voltage-gated calcium channel antibodies |
| **Myasthenia gravis** | • Thymoma | Acetylcholine receptor antibodies |
| **Hypercalcemia** | • Squamous cell lung cancer | Ectopic production of parathyroid hormone-related protein |
| **Dermatomyositis /polymyositis** | • Variable | Autoimmune |
| **Erythrocytosis** | • Renal cell cancer | Ectopic erythropoietin production |

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Hypercalcemia | cancer | parathyroid hormone-related



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This patient's lung mass, cerebellar symptoms, and autopsy findings are consistent with **paraneoplastic cerebellar degeneration**. This paraneoplastic syndrome is most commonly associated with small cell lung cancer as well as breast, ovarian, and uterine malignancies. Patients exhibit **progressively worsening dizziness, limb and truncal ataxia, dysarthria, and visual disturbances** (eg, diplopia, oscillopsia). Paraneoplastic cerebellar degeneration is due to an immune response against tumor cells that **cross-reacts with Purkinje neuron antigens**, leading to acute-onset rapid degeneration of the cerebellum. **Anti-Yo, anti-P/Q, and anti-Hu** are the most common antibodies detected in the serum. Antibodies are not always detectable; thus, paraneoplastic cerebellar degeneration is diagnosed clinically after excluding other conditions.

**(Choice B)** Some paraneoplastic syndromes occur due to the production of hormone-like substances from tumor cells, but these would not cause the neurological findings described in this case.

**(Choice C)** Acute cerebellitis (post-viral cerebellar ataxia) occurs most often in children 2-3 weeks following varicella, measles, or Epstein-Barr virus infection. It presents with cerebellar symptoms (eg, ataxia, nystagmus, dysarthria) that usually resolve completely within 3 weeks.

**(Choice D)** Cerebellar metastasis can cause progressively worsening subacute cerebellar symptoms. Additional findings such as headaches or decreased consciousness are often present due to significant



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ataxia, nystagmus, dysarthria) that usually resolve completely within 3 weeks.

**(Choice D)** Cerebellar metastasis can cause progressively worsening subacute cerebellar symptoms. Additional findings such as headaches or decreased consciousness are often present due to significant mass effect from the tumor. However, autopsy would show metastatic cancer cells with surrounding inflammation as opposed to Purkinje cell degeneration.

**(Choice E)** Adverse effects from systemic chemotherapy can include a wide range of neurologic complications. However, this patient's symptoms began before the lung mass was identified and his autopsy findings are more specific for subacute cerebellar degeneration.

**(Choice F)** Cerebellar infarction presents with vertigo, nystagmus, ipsilateral limb ataxia, and truncal lateropulsion (falling toward the lesion). Although repeated vascular events could result in a stepwise progressive loss in neurologic function, this process would most likely occur over several years and affect multiple vascular territories throughout the brain (causing a wide range of neurologic deficits). Autopsy would show areas of liquefactive necrosis (acute infarcts) and glial scarring (chronic infarcts).

**Educational objective:**
Paraneoplastic syndromes can occur due to the production of hormone-like substances from tumor cells. They can also result from immune reactions against tumor cells that cross-react with normal cells, causing


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inflammation as opposed to Purkinje cell degeneration.

**(Choice E)** Adverse effects from systemic chemotherapy can include a wide range of neurologic complications. However, this patient's symptoms began before the lung mass was identified and his autopsy findings are more specific for subacute cerebellar degeneration.

**(Choice F)** Cerebellar infarction presents with vertigo, nystagmus, ipsilateral limb ataxia, and truncal lateropulsion (falling toward the lesion). Although repeated vascular events could result in a stepwise progressive loss in neurologic function, this process would most likely occur over several years and affect multiple vascular territories throughout the brain (causing a wide range of neurologic deficits). Autopsy would show areas of liquefactive necrosis (acute infarcts) and glial scarring (chronic infarcts).

**Educational objective:**

Paraneoplastic syndromes can occur due to the production of hormone-like substances from tumor cells. They can also result from immune reactions against tumor cells that cross-react with normal cells, causing dysfunction and/or damage to healthy organs and tissues. Neurologic paraneoplastic syndromes (eg, paraneoplastic cerebellar degeneration) are an autoimmune phenomenon.

**References**

- Small-cell lung cancer, paraneoplastic cerebellar degeneration and the Lambert-Eaton myasthenic



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A 37-year-old previously healthy man comes to the office for evaluation of enlarged lymph nodes. He has an 8-week history of progressively enlarging cervical lymph nodes associated with subjective fevers, fatigue, and drenching night sweats. After initial assessment, the patient undergoes excisional biopsy of enlarged lymph nodes in the left posterior triangle of the neck. Two weeks later, during a follow-up visit, he describes difficulty with overhead activities such as combing his hair or placing dishes on overhead shelves. Examination shows a left shoulder droop with weakness of left arm abduction above 100 degrees. Other shoulder movements are normal, and there is no sensory loss. Which of the following muscles is most likely paralyzed in this patient?

A. Deltoid
B. Latissimus dorsi
C. Levator scapulae
D. Serratus anterior
E. Trapezius


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an 8-week history of progressively enlarging cervical lymph nodes associated with subjective fevers, fatigue, and drenching night sweats. After initial assessment, the patient undergoes excisional biopsy of enlarged lymph nodes in the left posterior triangle of the neck. Two weeks later, during a follow-up visit, he describes difficulty with overhead activities such as combing his hair or placing dishes on overhead shelves. Examination shows a left shoulder droop with weakness of left arm abduction above 100 degrees. Other shoulder movements are normal, and there is no sensory loss. Which of the following muscles is most likely paralyzed in this patient?

- A. ~~Deltoid~~ (17%)
- B. Latissimus dorsi (3%)
- C. ~~Levator scapulae~~ (9%)
- D. ~~Serratus anterior~~ (20%)
- ✓ E. Trapezius (48%)

Correct

48%

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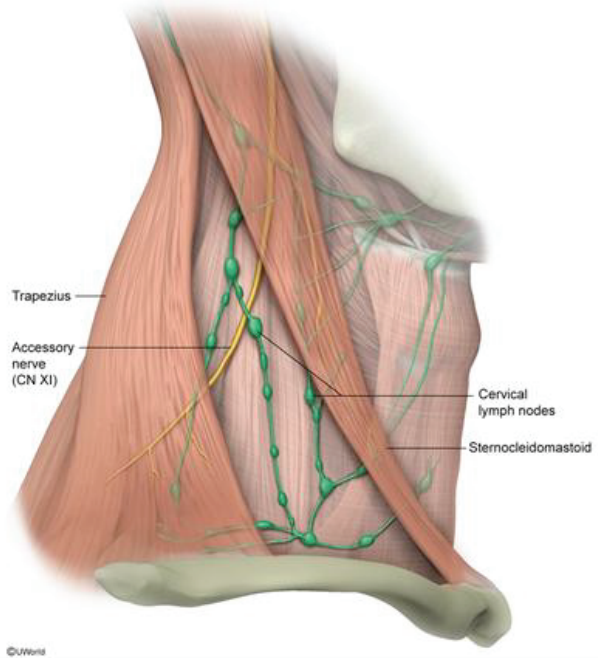
## Exhibit Display

Course of the accessory nerve in the neck

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The **spinal accessory nerve** (CN XI) is a pure motor nerve that innervates the sternocleidomastoid and trapezius. It follows a superficial course through the posterior triangle of the neck and is vulnerable to penetrating trauma and **iatrogenic injury** (eg, cervical lymph node dissection).

The trapezius elevates and rotates the scapula upward (eg, during arm abduction) and stabilizes the shoulder. Symptoms of trapezius weakness include **drooping of the shoulder**, impaired abduction of the arm **above 100 degrees**, and lateral displacement of the scapula. If the injury involves the proximal portions of the nerve, weakness of the sternocleidomastoid may also occur.

**(Choice A)** The deltoid is innervated by the axillary nerve (C5-6). Injury would cause impaired sensation over the lateral shoulder and weakness in abduction of the arm from 30 to 100 degrees. Iatrogenic axillary nerve injury can occur during shoulder surgery (eg, proximal humerus fracture repair) or intramuscular injection in the deltoid.

**(Choice B)** The latissimus dorsi is innervated by the thoracodorsal nerve which can be damaged during axillary lymph node dissection. It is the most powerful adductor of the arm and assists with extension and medial rotation.

**(Choice C)** The levator scapulae is innervated by the C3 and C4 cervical nerves and the dorsal scapular nerve (C5). It acts to elevate the scapula and rotate its medial border inferiorly but does not have a


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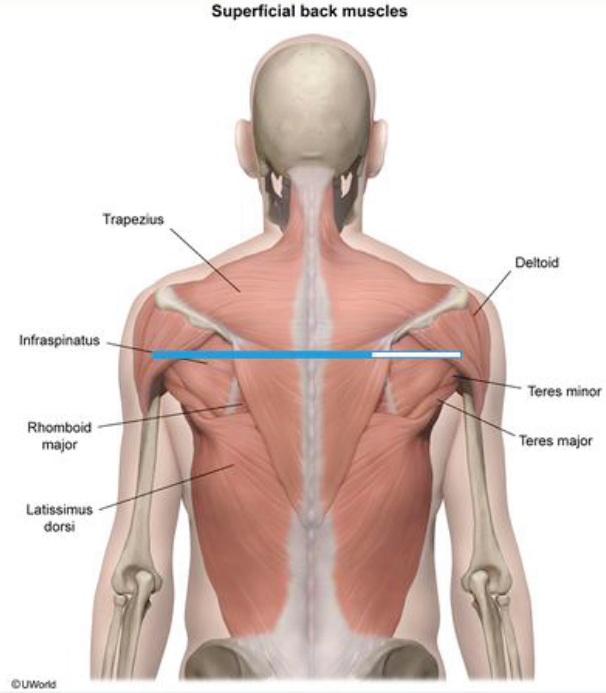


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injection in the deltoid.

**(Choice B)** The latissimus dorsi is innervated by the thoracodorsal nerve which can be damaged during axillary lymph node dissection. It is the most powerful adductor of the arm and assists with extension and medial rotation.

**(Choice C)** The levator scapulae is innervated by the C3 and C4 cervical nerves and the dorsal scapular nerve (C5). It acts to elevate the scapula and rotate its medial border inferiorly but does not have a significant effect on arm abduction.

**(Choice D)** The serratus anterior is innervated by the long thoracic nerve and protracts and rotates the scapula upward, assisting with elevation of the arm over the head. Although weakness of the serratus anterior causes winging of the scapula, it usually occurs following axillary lymph node dissection and would not be associated with shoulder droop.

**Educational objective:**
The spinal accessory nerve is vulnerable to injury in the posterior triangle of the neck. Injury results in weakness of the trapezius muscle, which presents with drooping of the shoulder, impaired abduction of the arm above 100 degrees, and lateral displacement of the scapula.


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A 36-year-old Caucasian male presents to your office complaining of periodic involuntary deviation of the head to the right, accompanied by muscle pain in his neck. The spells start spontaneously, last 30-40 minutes, and can sometimes be suppressed by placing a hand on the chin. This patient's condition can be best characterized as which of the following?

A. Myoclonus
B. Cogwheel rigidity
C. Bradykinesia
D. Chorea
E. Dystonia
F. Hemiballism

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A 36-year-old Caucasian male presents to your office complaining of periodic involuntary deviation of the head to the right, accompanied by muscle pain in his neck. The spells start spontaneously, last 30-40 minutes, and can sometimes be suppressed by placing a hand on the chin. This patient's condition can be best characterized as which of the following?

A. ~~Myoclonus~~ (26%)
B. ~~Cogwheel rigidity~~ (3%)
C. ~~Bradykinesia~~ (1%)
D. Chorea (6%)
E. Dystonia (55%)
F. Hemiballism (6%)

Correct

55%
Answered correctly

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Time Spent

10/23/2020
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**Dystonia** is a neurological movement disorder characterized by sustained, involuntary muscle contractions, which force certain parts of the body into abnormal, sometimes painful, movements or postures. These movements may affect a single muscle, a group of muscles, or the entire body. Dystonias may occur without any obvious cause (idiopathic).

Focal dystonias involve one muscle or a muscle group. Cervical dystonia, also called **spasmodic torticollis**, is the most common of the focal dystonias.

**Blepharospasm** is the second most common focal dystonia. It is an involuntary, forcible closure of the eyelids. The initial symptom is often uncontrollable blinking. Later, blepharospasm may cause complete closure of the eyelids. Another common type of focal dystonia is a **writer's cramp**, which affects the muscles of the hand.

**(Choice A)** Myoclonus is a sudden, brief, sometimes severe (shock-like) muscle contraction. Examples of physiologic myoclonus are hiccups and hypnic jerks (occur when falling asleep). Pathological myoclonus is seen in epilepsy and Creutzfeldt-Jakob disease.

**(Choice B)** On passive extension/flexion of a Parkinsonian limb, the examiner will feel intermittent resistance. This "ratchet-like" resistance to movement is called cogwheel rigidity.



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seen in epilepsy and Creutzfeldt-Jakob disease.

**(Choice B)** On passive extension/flexion of a Parkinsonian limb, the examiner will feel intermittent resistance. This "ratchet-like" resistance to movement is called cogwheel rigidity.

**(Choice C)** Bradykinesia means slow movement. It is also commonly seen in Parkinson disease.

**(Choice D)** Chorea is involuntary muscle activity that "flows" from one muscle group to another. Movements may appear fragmented or jerky, and the patient may display a "dancing" gait (Greek, chorea = dance). Chorea is a feature of Huntington disease.

**(Choice F)** Hemiballism refers to flinging of the limbs (arm and/or leg) on one side of the body. Hemiballism occurs due to contralateral injury in or near the subthalamic nucleus.

**Educational Objective:**
Dystonia is a syndrome of prolonged, repetitive muscle contractions. This condition may be the result of impaired function of the basal ganglia. Cervical dystonia (spasmodic torticollis), blepharospasm, and writer's cramp are the most common types of focal dystonia.

| Pathology | Nervous System | Dystonia |
|---|---|---|
| Subject | System | Topic |


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A 56-year-old woman is brought to the emergency department after a generalized tonic-clonic seizure witnessed by her husband. The patient has no history of seizures or other medical conditions but has been having recurrent headaches for the past several months. Physical examination shows mild weakness with increased deep tendon reflexes in the left upper extremity. MR imaging of the brain reveals a large mass in the right frontal lobe. Stereotactic biopsy of the mass yields hypercellular white matter with extensive astrocytic aberration, microvascular proliferation, and areas of necrosis lined by tumor cells. Molecular studies of the abnormal cells are most likely to demonstrate which of the following findings?

A. Abnormal tuberin and hamartin proteins
B. Constitutively active RET protein
C. Lack of merlin tumor suppressor protein
D. Overexpression of epidermal growth factor receptor
E. Presence of Epstein-Barr virus genome

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A 56-year-old woman is brought to the emergency department after a generalized tonic-clonic seizure witnessed by her husband. The patient has no history of seizures or other medical conditions but has been having recurrent headaches for the past several months. Physical examination shows mild weakness with increased deep tendon reflexes in the left upper extremity. MR imaging of the brain reveals a large mass in the right frontal lobe. Stereotactic biopsy of the mass yields hypercellular white matter with extensive astrocytic aberration, microvascular proliferation, and areas of necrosis lined by tumor cells. Molecular studies of the abnormal cells are most likely to demonstrate which of the following findings?

A. Abnormal tuberin and hamartin proteins (10%)
B. Constitutively active RET protein (16%)
C. Lack of merlin tumor suppressor protein (18%)
D. Overexpression of epidermal growth factor receptor (51%)
E. Presence of Epstein-Barr virus genome (2%)

51%
01 min, 47 secs
12/14/2020


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This patient's seizure, headache, motor weakness, and brain mass composed of abnormal astrocytes with necrosis and microvascular proliferation raises strong suspicion for **glioblastoma** (GBM), a highly aggressive tumor that stems from **glial** or pluripotent neural stem cells. A number of characteristic oncogenic mutations are usually present in GBM, but >95% of cases are associated with the overexpression of **epidermal growth factor receptor (EGFR)** on the surface of neoplastic cells.

EGFR is a tyrosine-kinase signal transduction system that conducts external growth signals into the nucleus, thereby **promoting cellular survival** and proliferation. Mutations that enhance this pathway (eg, overexpression of EGFR or EGFR-ligand) are associated with uncontrolled cellular proliferation and are seen in GBM and other cancer types (eg, non–small cell lung cancer, breast cancer, prostate cancer). Therefore, drugs that inhibit the EGFR/EGFR-ligand interaction (eg, erlotinib) are often used as part of treatment.

**(Choice A)** Tuberous sclerosis is an autosomal dominant disorder associated with abnormal tuberin and hamartin. It generally causes benign tumors in the skin (eg, ash-leaf lesions, angiofibromas), central nervous system (eg, subependymal giant cell astrocytomas [SEGA]), and other tissues. SEGA commonly presents as an intraventricular mass composed of large cells with abundant eosinophilic cytoplasm; necrosis and microvascular proliferation would be atypical.


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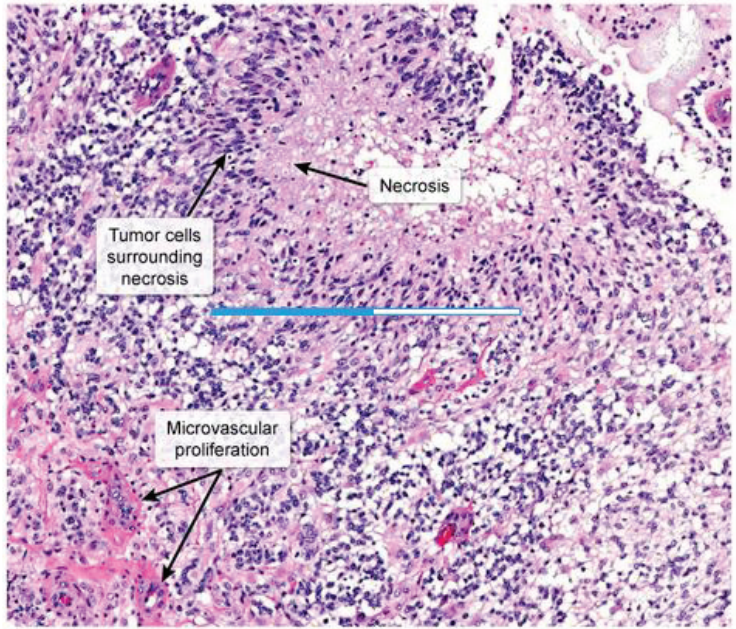
Glioblastoma

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necrosis and microvascular proliferation would be atypical



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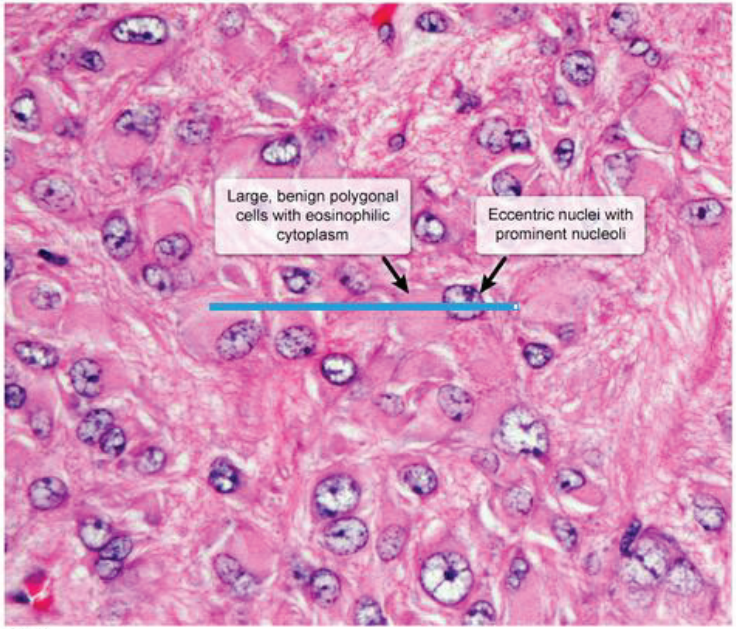
Subependymal giant cell astrocytoma (tuberous sclerosis)

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necrosis and microvascular proliferation would be atypical



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necrosis and microvascular proliferation would be atypical.

**(Choice B)** Multiple endocrine neoplasia type 2 is an autosomal dominant disorder associated with constitutive activation to the RET proto-oncogene, leading to increased risk for medullary thyroid cancer, pheochromocytoma, and hyperparathyroidism. GBM is not classically linked to RET protein alterations.

**(Choice C)** Neurofibromatosis type 2 is due to mutations that inactivate the merlin tumor suppressor protein. It is associated with vestibular schwannomas and meningiomas; patients may also have eye and skin lesions. A frontal lobe mass would be unusual.

**(Choice E)** In immunosuppressed patients, primary CNS lymphoma often expresses Epstein-Barr virus (EBV) genes and is thought to be linked to EBV reactivation in B lymphocytes (the site of latent infection). However, biopsy would reveal atypical lymphoid cells, not astrocyte aberration.

**Educational objective:**
Glioblastoma is an aggressive primary brain neoplasm that generally presents with slowly worsening headache, seizure, and/or focal neurologic issues. Most cases are associated with oncogenic mutations that increase epidermal growth factor receptor expression on the tumor cells, leading to increased transduction of growth signals that promote cellular survival and proliferation.


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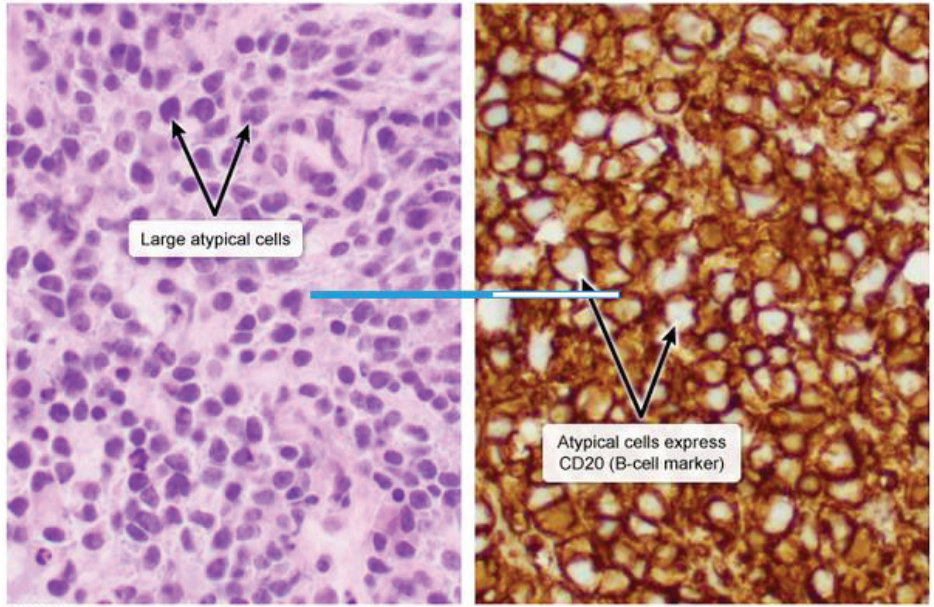
Primary CNS diffuse large B-cell lymphoma

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A 45-year-old woman comes to the emergency department due to sudden-onset, severe headache. On arrival, the patient is alert and oriented and has no focal neurological deficits. CT scan of the head reveals subarachnoid hemorrhage, and she is admitted to the critical care unit. Over the next several hours, the patient gradually becomes somnolent and less responsive. She opens her eyes to painful stimuli only and does not follow commands. Repeat imaging of the brain shows no new hemorrhage, but there is enlargement of the entire ventricular system compared to the previous CT scan. Which of the following is the most likely cause of this patient's neurologic deterioration in the hospital?

A. Blockage of the cerebral aqueduct by blood products
B. Cerebral vasospasm due to subarachnoid blood
C. Edema from a disruption in the blood-brain barrier
D. Excessive production of cerebrospinal fluid
E. Impaired absorption of cerebrospinal fluid

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A. ~~Blockage of the cerebral aqueduct by blood products~~ (20%)
B. Cerebral vasospasm due to subarachnoid blood (20%)
C. ~~Edema from a disruption in the blood-brain barrier~~ (5%)
D. ~~Excessive production of cerebrospinal fluid~~ (0%)
E. Impaired absorption of cerebrospinal fluid (52%)

52%
01 min, 39 secs
02/15/2021


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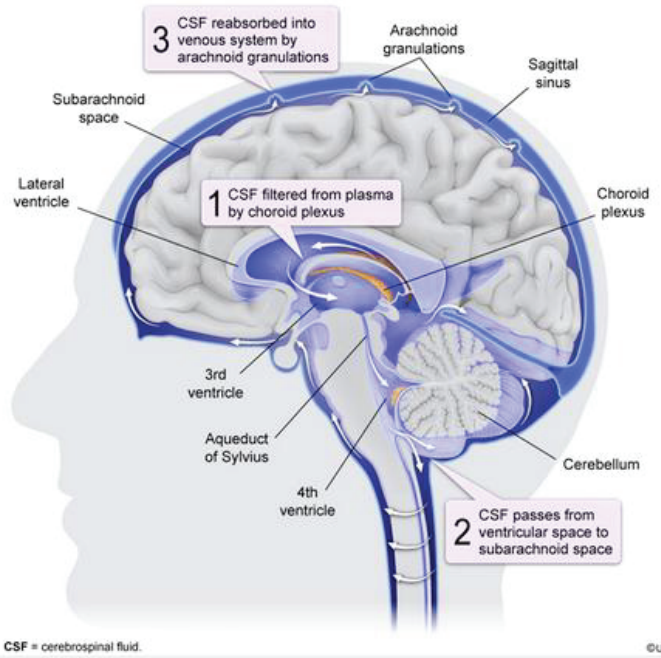
Flow of cerebrospinal fluid




CSF = cerebrospinal fluid.

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CSF = cerebrospinal fluid.

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**Hydrocephalus** is a common complication of **subarachnoid hemorrhage** (SAH). Blood in the subarachnoid space can acutely obstruct and **impair absorption** of cerebral spinal fluid (CSF) by the **arachnoid granulations**. Later, blood-induced inflammation can cause fibrosis of the arachnoid granulations that perpetuates the absorption impairment and leads to chronic hydrocephalus.

Impaired CSF absorption creates a **communicating** hydrocephalus. Because the blockage to flow is distal to the entire ventricular system, **enlargement of all 4 ventricles** occurs. The ventricular enlargement stretches adjacent nerve fibers and, in the acute setting, leads to **deteriorating mental status** (eg, somnolence, unresponsiveness). Treatment involves the placement of an external ventricular drain to relieve pressure in the ventricular system and subarachnoid space. Patients who develop chronic hydrocephalus may require placement of a permanent shunt (eg, ventriculoperitoneal shunt).

**(Choice A)** Blockage of the cerebral aqueduct (aqueduct of Sylvius) is less common with SAH and more typically occurs with intracerebral hemorrhage complicated by intraventricular bleeding. The resulting hydrocephalus is noncommunicating as there is no free passage of CSF from the ventricular space into the subarachnoid space. Enlargement of only the lateral and third ventricles is expected; the fourth ventricle is distal to the obstruction and remains normal in size.

**(Choice B)** Cerebral vasospasm is a common complication of SAH; however, it is typically delayed



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**CSF** = cerebrospinal fluid.

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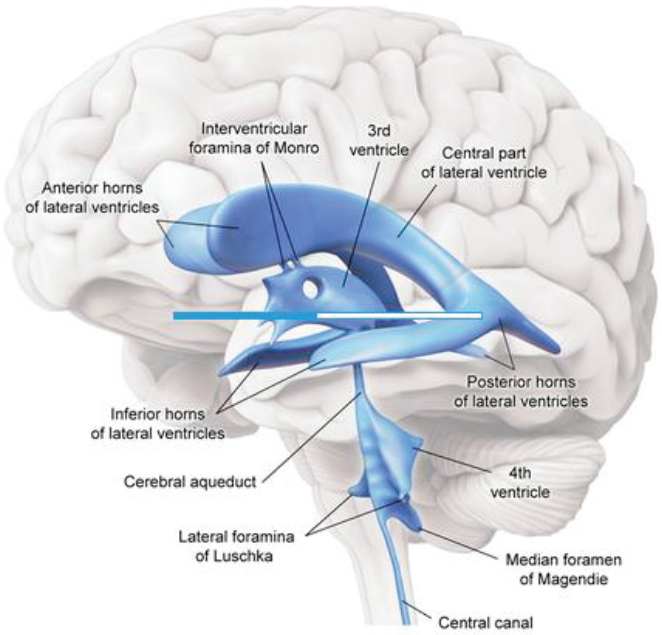
## Exhibit Display

### Ventricular system

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**(Choice B)** Cerebral vasospasm is a common complication of SAH; however, it is typically delayed



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**(Choice B)** Cerebral vasospasm is a common complication of SAH; however, it is typically delayed, occurring 4-14 days following the initial bleed, and leads to localized stroke with focal neurologic deficits rather than deteriorating mental status. Dilated ventricles are not seen.

**(Choice C)** Edema that occurs due to disruption of the blood-brain barrier (vasogenic cerebral edema) collects within the brain parenchyma and can result from stroke or trauma. It is not expected following SAH.

**(Choice D)** Excessive CSF production is a rare cause of communicating hydrocephalus that may result from a choroid plexus papilloma. Enlargement of all 4 ventricles is expected, but this patient's SAH makes impaired absorption of CSF far more likely.

**Educational objective:**
Communicating hydrocephalus is a common complication of subarachnoid hemorrhage that presents with deteriorating mental status. It typically results from blood-induced impairment of absorption of cerebrospinal fluid by the arachnoid granulations.

**References**

- Predictors of ventriculoperitoneal shunting following subarachnoid hemorrhage treated with external ventricular drainage.


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A 68-year-old woman comes to the emergency department for evaluation of stroke-like symptoms. The patient says her face appeared "twisted" this morning but was normal when she went to bed last night. Her brother recently had a stroke, and she was worried that she may also be having a stroke. The patient has a history of hypertension, hyperlipidemia, and type 2 diabetes mellitus. Vital signs are within normal limits. Physical examination shows facial asymmetry with drooping of the left corner of the mouth and loss of the left nasolabial fold. Which of the following additional examination findings on the affected side would be most suggestive of central nervous system involvement?

A. Decreased eye lacrimation

B. Inability to tense soft tissues of the neck

C. Increased loudness of sounds

D. Loss of taste sensation on the anterior tongue

E. Sparing of the forehead muscles

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A 68-year-old woman comes to the emergency department for evaluation of stroke-like symptoms. The patient says her face appeared "twisted" this morning but was normal when she went to bed last night. Her brother recently had a stroke, and she was worried that she may also be having a stroke. The patient has a history of hypertension, hyperlipidemia, and type 2 diabetes mellitus. Vital signs are within normal limits. Physical examination shows facial asymmetry with drooping of the left corner of the mouth and loss of the left nasolabial fold. Which of the following additional examination findings on the affected side would be most suggestive of central nervous system involvement?

A. Decreased eye lacrimation (7%)

B. Inability to tense soft tissues of the neck (4%)

C. Increased loudness of sounds (6%)

D. Loss of taste sensation on the anterior tongue (8%)

✓ E. Sparing of the forehead muscles (72%)

72% 53 secs 03/20/2021


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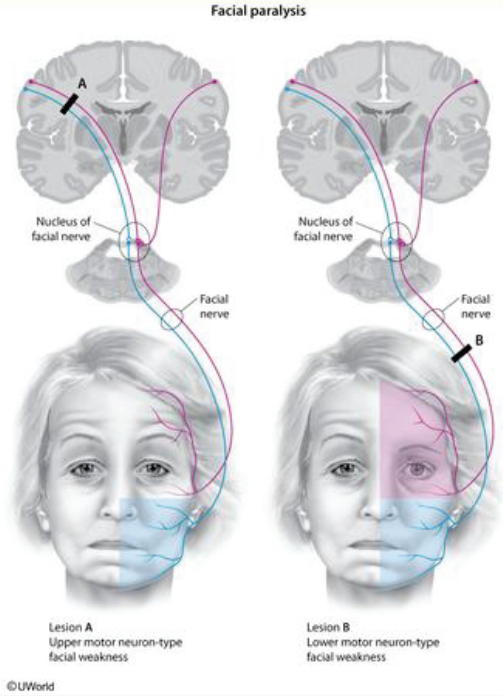


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Voluntary facial movement is initiated by the motor cortex (located in the frontal lobe), which delivers input to the facial nerve (CN VII), a peripheral nerve that innervates the muscles of facial expression. Central or peripheral lesions can often be distinguished by assessing movement in the upper face.

- **Central nervous system lesions** (eg, stroke) typically affect the motor cortex or the descending tracts; this results in contralateral lower face weakness. However, the nuclei that innervate the **upper face** receive **bilateral input** from the motor cortices, so movement of the upper facial muscles (eg, forehead, brow) is often **spared**.
- **Peripheral nerve lesions** (eg, Bell palsy) affect the entire facial nerve. This results in unilateral weakness of half of the face; **forehead movement is lost**.

The most common cause of acute unilateral upper and lower facial weakness is **Bell palsy**, an acute peripheral neuropathy of **CN VII**. Common findings include an inability to raise the eyebrow or close the eye, drooping of the mouth corner (with the mouth drawn to the unaffected side), and disappearance of the nasolabial fold. For most patients, partial or complete recovery occurs within 3-4 months.

**(Choices A, C, and D)** Patients with facial nerve lesions often have decreased tear production (due to loss of parasympathetic innervation to the lacrimal gland), hyperacusis (due to weakness of the stapedius


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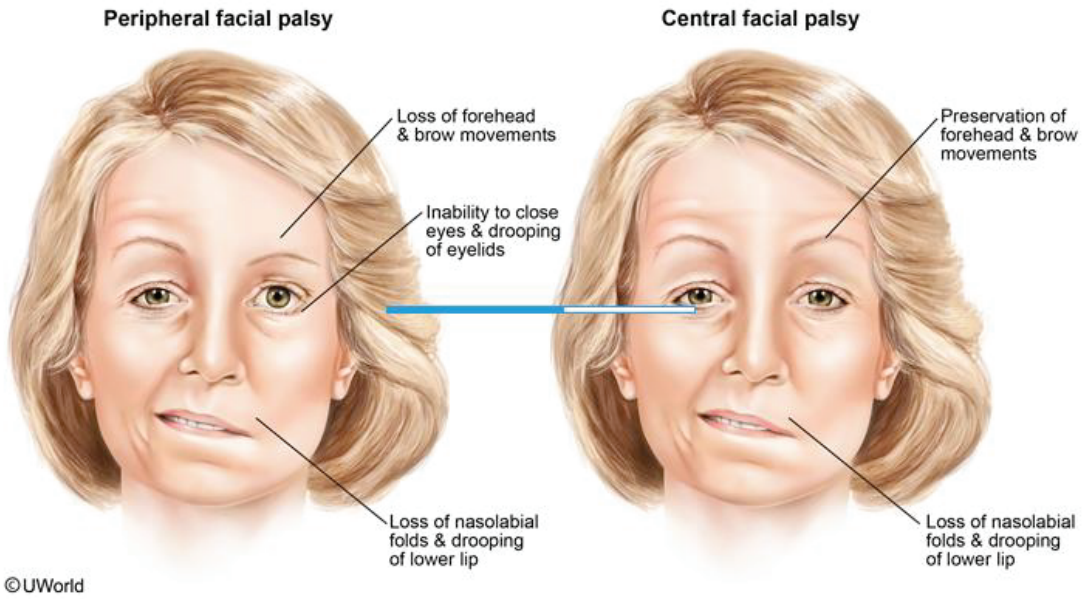


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**(Choices A, C, and D)** Patients with facial nerve lesions often have decreased tear production (due to loss of parasympathetic innervation to the lacrimal gland), hyperacusis (due to weakness of the stapedius muscle), and decreased sensation of taste over the ipsilateral anterior two-thirds of the tongue (which is innervated by the chorda tympani nerve, a branch of the facial nerve).

**(Choice B)** The platysma muscle, responsible for tensing the skin on the neck, is also innervated by the facial nerve. It would be affected in both central and peripheral lesions.

**Educational objective:**

Because the upper face receives bilateral input from the motor cortices, central nervous system lesions typically cause unilateral lower facial weakness that spares the forehead. In contrast, peripheral lesions (eg, Bell palsy) cause weakness of the entire side of the face. Bell palsy may also result in decreased tear production, hyperacusis, and reduced taste sensation.

**References**

- Bell's palsy.

| Pathophysiology | Nervous System | Bell's palsy |
|---|---|---|
| Subject | System | Topic |


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A 3-week-old boy is evaluated in the neonatal intensive care unit due to apnea. The patient was born at 27 weeks gestation and had a birth weight of 1 kg (2 lb 2 oz). For the past 2 weeks, he has been stable on minimal respiratory support via nasal cannula but has had intermittent episodes of no respiratory effort for up to 30 seconds at a time. These episodes are associated with bradycardia and desaturation. The patient recovers spontaneously or with brief stimulation from the nurse. He is well appearing between episodes. Examination of the lungs reveals bilateral, clear breath sounds with easy work of breathing. Ultrasound of the head is normal. Arterial blood gas values are normal. This patient's clinical findings are most likely caused by an abnormality in which of the following areas?

A. Central stimulatory neurons
B. Lower motor neurons
C. Mixed motor sensory nerves
D. Peripheral chemoreceptors
E. Pulmonary stretch receptors


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weeks gestation and had a birth weight of 1 kg (2 lb 2 oz). For the past 2 weeks, he has been stable on minimal respiratory support via nasal cannula but has had intermittent episodes of no respiratory effort for up to 30 seconds at a time. These episodes are associated with bradycardia and desaturation. The patient recovers spontaneously or with brief stimulation from the nurse. He is well appearing between episodes. Examination of the lungs reveals bilateral, clear breath sounds with easy work of breathing. Ultrasound of the head is normal. Arterial blood gas values are normal. This patient's clinical findings are most likely caused by an abnormality in which of the following areas?

- ✓ A. Central stimulatory neurons (100%)
- B. ~~Lower motor neurons~~ (0%)
- C. ~~Mixed motor sensory nerves~~ (0%)
- ✗ D. Peripheral chemoreceptors (0%)
- E. ~~Pulmonary stretch receptors~~ (0%)

Incorrect
Correct answer

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Time Spent

03/31/2021
Last Updated



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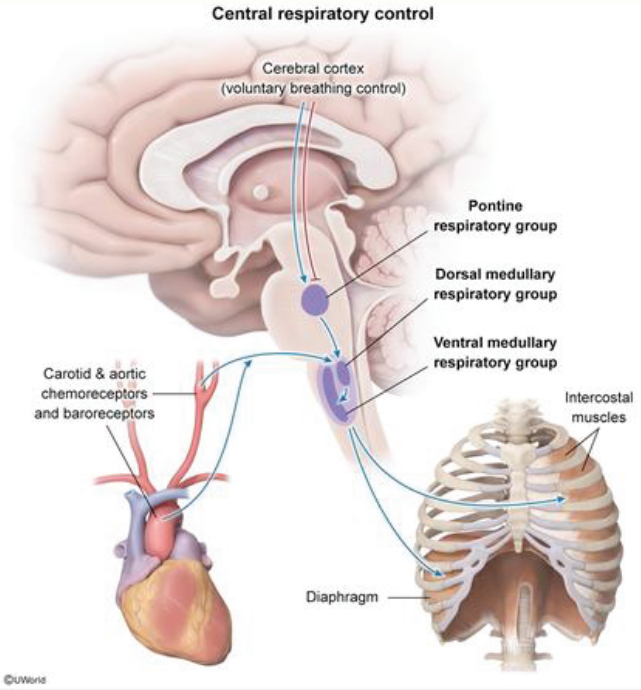


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Apnea is defined as episodes of **respiratory cessation** lasting >20 seconds, often associated with decreased heart rate and oxygen saturation. Apnea may be obstructive, in which respiratory effort occurs but is blocked, or central, which is characterized by the absence of any respiratory effort. This patient has **apnea of prematurity**, a type of central apnea that occurs in virtually all extremely preterm newborns at gestational age <28 weeks due to **immature** central respiratory centers.

The normal respiratory drive originates from respiratory centers in the pons and medulla. The **medullary respiratory centers** are stimulatory neurons that trigger inspiration (from the dorsal respiratory group) and expiration (from the ventral respiratory group). These neurons send impulses to the diaphragm via the phrenic nerve and to the intercostal muscles. The medullary respiratory centers receive input from the **pontine respiratory centers**, which receive constant feedback from chemoreceptors, stretch receptors, and proprioceptors to modify respiration. In addition, the respiratory centers can be consciously overridden by the cortex (eg, intentional deep sigh, breath-holding).

In apnea of prematurity, the central stimulatory neurons are not fully developed, leading to intermittent interruptions in the normal respiratory drive. Apneic episodes typically develop within the first few days of life and may persist for up to several months while the central respiratory centers mature. Treatment is with methylxanthines (eg, caffeine), which stimulate respiratory neural output.


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**(Choices B and C)** Failure of the lower motor neurons (that innervate the intercostal muscles) or mixed motor sensory nerves, such as the phrenic nerve (that innervates the diaphragm), can cause apnea in conditions such as spinal muscular atrophy type 1 or phrenic nerve injury, respectively. This newborn has normal breathing between episodes, which makes nerve impairment unlikely.

**(Choice D)** Peripheral chemoreceptors (eg, carotid bodies, aortic body) sense changes in carbon dioxide, oxygen, and pH levels and trigger the central respiratory center to modify respiration. This patient's laboratory findings show normal blood gas values, so respiratory changes are not being driven by chemoreceptors.

**(Choice E)** Stretch receptors in the lung trigger cessation of inspiration when the lung is approaching total lung capacity. This newborn has normal respiration between episodes and is not hyperexpanding the lungs, so the stretch receptors are not involved in his apnea.

**Educational objective:**
The pontine and medullary respiratory centers coordinate normal respiratory drive. Immaturity of these central respiratory centers causes apnea of prematurity, which is common in extremely preterm newborns.

Physiology Nervous System Respiratory physiology


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